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## Part I.—Original Articles

### THE AETIOLOGY OF SCHIZOPHRENIA IN CHILDHOOD.

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THE aetiology and significance of schizophrenia in childhood is still so obscure that it is profitable to analyse fully every case that is diagnosed. In the United States of America, where cases appear to occur more frequently, the picture of full-blown childhood schizophrenia has been well drawn by Bender, Kanner, Szurek and others, but the descriptions are more of the whole forest and the details of the individual tree are missed in the whole. Excellent individual studies certainly are made, but the significance is often not understood, as if the workers were more used to macroscopic than to microscopic studies, but an unforgettable demonstration of the gross pathology and clinical picture of childhood schizophrenia is given at the Langley Porter Clinic in San Francisco. The over-all impression is one of emotional fixation at the infant to toddler level. In a variety of cases all stages may be shown from the oral to the anal level of erotism, from the delight and practice of bodily movements at rest and in space, to the experiments and flights in fantasy of the later period. Play is also at the toddler or earlier level—one child of ten years came offering everyone cups of imaginary coffee to drink—and there is the same lack of team spirit, the same failure to make groups of more than two for any length of time, the same mischievous exploratory tendency, the same perseveration tendency with any trick, the same range of comfort mechanisms from thumb-sucking to rocking and masturbation, the same range of speech from babble to sentences as is found in any nursery and nursery school, although the chronological age-range may be five to fifteen years instead of six months to five years.

In Britain, however, where the number of cases is so limited that there are still psychiatrists who would hesitate from personal experience to diagnose a case, we can savour the individual case and submit it to a microscopic analysis, hoping so to understand this entity that we may prescribe the most appropriate treatment. Creak has recently urged a greater accuracy in the whole study of these children. I venture therefore to put before you a case which has been studied in detail, a typical case, which demonstrates most of the points on which I base my hypotheses of the aetiology.

The patient was a girl within a month of her seventh birthday when she first came to the clinic, brought by her mother at the instigation of the Education Authorities, as she was "backward, maladjusted and showed abnormal sexual behaviour." Her mother, who was a postwoman of average intelligence, gave an astute account of the child, who she said was driving them all mad at home. The girl was backward at school, but the mother said that she *behaved* at home like a child of three or four. She was extremely erratic, frequently unco-operative and spasmodically aggressive. She required much persuasion to eat, would not carry out requests or commands, was frequently involved in fights, for she tormented other children, and if thwarted she would react violently, throwing everything about the place. She was much worse in the mornings, when she would scatter the bedclothes all over the house.

Physically she was very restless, running, jumping and swinging. She refused to sit constantly at table, but jumped up and down, and to this habit was attributed her indigestion, hiccoughs and occasional stomach pains. She had aggressive phases of biting and scratching, but most concern was expressed about her excretory habits. She has suffered from "dysentery," and until a few months before had had no control over her bowels. She was still enuretic in her restless sleep. Her worst fault, however, was her insistence upon using the boys' lavatory at school in spite of correction and physical punishment, and she brought shame to her mother by micturating in a standing position in the street.

The psychologist was unable to test this child properly, but estimated the Intelligence Quotient (Terman Merrill Form L) to be in the eighties, which gave her a mental age of at least 5½ years. She looked more vacant than this intelligence might suggest, and although brightly dressed was unprepossessing. She had a severe lalling speech defect of which neither the school nor the mother had complained. At the initial interview she behaved like a child of 2½ to 3 years, showing no shyness but running round opening cupboards, investigating drawers and lifting the telephone. She answered inappropriately, and volunteered information about boys and their activities which were denied to girls. In telephone play she showed at first a tendency to echolalia; but later through the telephonic medium she was able to answer questions more appropriately, saying that she wanted a doctor for her little boy who had had his leg cut off. As soon as she had said this, she ran crying from the room and buried her face in the male psychologist's leg like a hurt toddler seeking protection from father. She resumed her activities suddenly, enjoying being rocked by the nurse, swinging on ledges not intended for this activity, jumping on chairs, and again speaking on the telephone, the mouthpiece of which she afterwards sucked.

Her spontaneous drawings showed the lack of persistence of purpose typical of the schizophrenic. They were impulsively executed and seemed to mean nothing to her afterwards. Yet on the Rorschach Test she showed that she could produce adequate images where the form was precise, e.g., butterflies and Christmas tree; and on the Goodenough Drawing Test she achieved 9 points (mental age 5½). From the Rorschach Test it was concluded that she was not defective but disturbed, showing abnormal behaviour, and having poor powers of concentration with fleeting attention. Her E.E.G. was slightly abnormal with an alpha rhythm of 8 to 10 per second, but with too much 4 to 6 per second slow wave abnormality to be within normal limits for her age.

Her play demonstrated a severe emotional disorder. Play with boy dolls in connection with the lavatory rapidly suggested death involving not just the offender but all. She destroyed her own image for enuresis, and promptly killed everything else in the room except the policeman. Her play had bizarre trends. She would perform ritualistic movements, suddenly crouching or curtseying with no apparent relationship to the rest of her play, and she once *planted* two girls (dolls). She also demonstrated visibly her concrete thinking, e.g., a burglar had climbed on to the roof of the house, forced an entry, and killed everyone. The policeman collected all the bodies into the *living* room so that they would come *alive* again. Instead of pretending to drink, as would others of her age, she would really drink the dirty play water in spite of repeated correction by the real toddlers in the room. She behaved impulsively, especially with other children, and once tore a rubber mat and began to eat it.

The ritualistic performances stopped after two months. She began to climb to unsafe places normally ignored by other children because of their unsuitability. She frequently demonstrated this inability to appreciate the realities of her environment, pointing Melanie Klein's statement of schizophrenic children in general that the ego has ceased to form a relationship with reality. Later she began to be inquisitive about the therapist's under-clothes and finally demanded to see her "Willy." She continued to claim that she was a boy, would micturate in a standing position, observed by the nurse who was screened from the child's view, and in the Terman Merrill memory test refused to repeat "I am a big girl" but substituted for "girl" the word "boy."

Her speech improved slightly, but there was no consistent improvment in her behaviour. She began to wander into other people's houses, saying that she was lost, although she really knew her address. She also insisted always that she was five years old, although she knew that she was seven. She was discovered

pulling at her small cousin's penis as if wanting to tug it off. As she was socially so difficult she was removed to an institution.

This is not an isolated case, and is comparable with those mentioned by Creak in her recent article on " Psychosis in Childhood." It is paralleled by Bender's and Kanner's cases. The child presented a picture typical of schizophrenia. The general impression was of the inquisitive toddler, still at the baby-talk stage and not fully in touch with reality. She gave evidence of concrete thinking, and desired more concrete proof than would be expected for her age. Her behaviour therefore was incongruous, bizarre, and her responses to reality situations not appropriate. She appeared to be deluded, believing that she was a boy, using boys' latrines and putting on the boys' clothes in the school cloakroom. It was interesting to note in this case the origin of bizarre behaviour based on concrete premises. For example she believed that she was a boy but that she had no penis. Her cousin had a penis which she tried to pull off, presumably to attach to herself. This behaviour might have been within normal limits if her chronological age had been 2½ to 3 years, but this child was seven years old. We may note in this case the retardation of emotional development to less than half the chronological age and a persistence of a concrete outlook more appropriate to the 2½-year period, both retardations being greater than even the estimated intellectual defect.

The cause and further evidence of this retardation must be sought in the past history. The child was derived from a father recognized in the neighbourhood as " dotty." He appears to have been a shy, retiring man, socially very backward and with marked obsessions. He would walk along one side of the street, walk back, cross the street and walk along the opposite side as a ritual to approaching his home. This man, a miner, was killed in a pit accident when the child was eight months old, so that she could not have been environmentally infected by his behaviour. The mother, some eight years younger than the father, is over-conscientious and immature, very dependent upon her own mother. Three years before the child was born she had suffered from gastric ulcer. She has bouts of depression and dermatitis, and frequent migrainous headaches. Not one of her mother's four children could be called a normal life, although she herself at the age of thirty-three gave to the world an appearance of normality except that she looked twelve years older than her chronological age. One sister had died of meningitis in adolescence. A sister suffered from epilepsy, and a left-handed brother was a chronic chest sufferer. The father's family was reported as non-pathological but obviously the informant had never regarded it critically. There were twins on both sides of the patient's forbears but the patient herself was the only child of the union.

The mother, however, had had two children from a previous marriage to a bigamist. These two girls (aged 12 and 9 years) did not come into the picture much in spite of the fact that they lived under the same roof as the patient, who behaved like an only child. The mother had married the patient's father very quickly after the discovery of the bigamous alliance. During the pregnancy she became worried about her sister's epilepsy and she felt over busy, for she cared for her two children excessively, making all their clothes as well as attending to the house-work and cooking. She appears to have accepted the labour nonchalantly, but two days after the birth, which had taken place in the maternal grandmother's home, she rose while her own mother was out and began to do the housework. She was very depressed and unwell, and did not lose this malaise and dizziness for a whole year. The child's father was killed eight months after the birth, so that the mother with little time to recover from her grief had to go out to work while the three children were left to the care of the grandmother.*

The patient, from conception, therefore, had suffered from maternal deprivation. The maternal worry and restlessness may have had an effect on the foetus, for it has been found at the Fels Institute, Yellow Springs, Ohio, that restless mothers produce restless babies. The mother gave only the simplest care to the child after birth, for she had little energy to spare. The baby was left outside in all weathers and handled only for feeding and bathing. There seems to have been no indulgence in fondling or nursing, although the father " played " with the

* Note that both parents came from working-class stock as, indeed, I have found in all my cases except one. This is in contrast to Kanner's finding that this psychosis occurs more in the highly intellectual, professional levels.

child occasionally in the evenings. Later I shall refer to the importance of this. After the age of six months she was allowed to cry herself to sleep, and from the age of eighteen months she passed from individual to community care by day in a day nursery, nursery school and later school, so that her mother might more easily carry out her duties as postwoman.

The child's reactions even at an early stage were not really appropriate to the environment. She was born a month prematurely but weighed 6¼ lb. and the labour was quite normal. Her immediate recovery from the birth was good, but three days later she went blue for about an hour. While fed on the breast in the first month she prospered, uninfected by the mother's depression, and it was only with the failure of the maternal milk that trouble began. Kanner has noted the frequency of these early feeding difficulties. She objected strongly to the bottle and failed to thrive well on Ambrosia. She weaned quickly, beginning at six months, and enjoying her new foods although she tended to become fixed on one type, e.g., for a period she refused everything but Quaker Oats. She was late in cutting her teeth, for the first two did not appear until a year and two months and no more came until she was two years; the rest followed rapidly accompanied by bouts of feverishness. She was late in walking, at a year and ten months, and with even the rudiments of speech (2 years). She did not become comprehensible to outsiders until she was six years old.

Her behaviour is interesting. In the first six months, in spite of her restless pregnancy and the mother's depression, she was considered almost too good to live. She lay contentedly in her pram outside all day. At six months, however, she began to be cross, especially at night, and during the day she would throw everything out of the pram fretfully. This change was unrelated to the environmental atmosphere. The Health Visitor remembers her as healthy, plump and clean and no problem; yet the mother insists that just before the father died the child had become "naughty," crying perpetually. Her "tantrums" continued into toddlerhood. She climbed out of her cot, and before she could walk would wander as far as an adult could travel in a quarter of an hour.

Her reactions to the nursery are not noted, but although she liked the nursery school to which she went at two years, she was considered difficult. She was dirty in her habits and had bouts of diarrhoea and constipation. Others would not play with her as she was restless and wanted everything. Just before she was five years she went to her present school, where she was considered to be all right in the nursery class but later proved to be a severe problem. She has always required a great deal of attention, for she is given to impulsive behaviour, and recently cut off her hair. She has always been hypersensitive to criticism by mother figures and has had to be much comforted. Recently, too, she has been acknowledging all men as "Daddy"—an early toddler trait.

Unlike the typical mental defective she has contracted few illnesses, having only measles and chicken-pox on her list; and in spite of her impulsive behaviour she has had no accidents. Judging from her outward responses she has had neither fright nor trauma.

Here then is the factual summary of this child and her environment. At the age of seven years she presented a schizophrenic picture with bizarre behaviour, apparently dependent upon her concrete thinking processes, and one delusion that she was a boy without a penis. This in itself is the concrete realization of the abstract phantasy experienced by most little girls over a varying, often fleeting, period in toddlerhood. This child had great difficulty with abstract thought, and required concrete evidence of those facts which most children of her age can visualize, without having seen them, by a process of deduction. This child had no image of the body under the clothes. She also seemed unable to visualize what her own body would do before the event. The mobile component of her own body image was missing.

From the behaviour of a child from 2 to 4 years, and possibly even younger, it can be concluded that the child has a body image that moves and has feelings. On the basis of this image the child is able to calculate that it would like to do certain things, make certain movements, because these actions would give pleasure or satisfaction to a part or the whole of its body. The patient seemed to have an inadequately formed body image, and having no basis for calculation, she moved impulsively and reacted without expectation of a result.

Little work has been done on the rate of formation of the body image and

its correlation with intellectual and emotional growth. The formation of the body image is probably the first step in abstract thinking. By means of this experience, the ability to visualize even those parts of the body which we cannot see, we are able to form images of other living creatures so that we can know that they are there, even when they or parts of them are invisible. A baby of seven to ten months may cry when its mother leaves the room for it has no image of her. Until that time it has been satisfied with the perceptual level, but it is growing to the conceptual level where images are necessary. Most striking was an experience that I had with a child of a year and three months. This little boy was intrigued with the novelty of his first feel of the sea-shore. He laughed at our dog, who also was enjoying the outing and who leaped with abandon into a deep pool. The child's laughter changed to a scream of terror which we could not, at first, understand; but, on looking at the picture with the child's eyes, concretely, we saw a decapitated dog's head floating on the water, the rest of the child's playmate having quite disappeared. Another child of two and a half was not at all disturbed, for she had the image of the dog still attached to its visible head.

The static body image might be counted as formed when the child can appreciate its own image in a mirror. Babies at the perceptual level, around six months, are not interested in this picture. A little later they may evince puzzlement or interest as in another child. Only when their own body image is formed (approx. 7 to 10 months) can they take a narcissistic pleasure in viewing themselves and recognizing themselves. These stages can be seen perhaps more clearly in domestic animals, where each stage lasts a longer time.*

Preoccupation and difficulty with mirror images is well recognized in schizophrenic children. The Langley Porter Clinic in San Francisco showed family ciné films of a child's life showing the schizophrenic patient at the age of three years and four months puzzled and interested in herself in the mirror, whereas most children can recognize themselves by one year. In my patient there was no record of this stage of her development or of preoccupation with her image, possibly because she comes from a stratum of society that has little or no contact with a mirror.

In schizophrenic children I would postulate that there is always a delay in the formation of the body image with consequent delay in general image formation, and therefore retardation or arrest in development of abstract thinking. The formation of the body image is at an intuitive rather than a perceptual level, dependent upon general rather than specific sensation, such as is registered by the nerve-endings in the muscles and skin. It travels to the higher centres via the posterior columns and the thalamus. Neurological defect of any part of the paths would give rise to delay or even deformity in formation of the body image. The skin corpuscles can be seen as early as the third foetal month, and the major pathways entering and leaving the thalamus are (according to Streeter) apparent by the end of the second month. The neuro-muscular and tendon endings are not to be seen until midway in the foetal existence, but their final characteristic course in relation to particular muscles is not plotted until much later. As yet we know very little about the factors affecting foetal development, but from the work of Sontag in the Fels Institute it is reasonable to suppose that an overactive mother might affect adversely the neurological "finish" of her child, since there is evidence to show that hyperactive foetuses dwell in overactive mothers, tend to be fat-impoverished after birth and to remain over-active, with postnatal bowel and sleep disorders.

It is possible therefore that my patient may have had a general and mild defect of the touch, pain, temperature and position sense tracts from birth, especially as she comes of a family with neurological abnormalities, left-handedness, epilepsy and migrainous manifestations, and emotional peculiarities. After birth, however, we are on surer ground. Russell Brain, in his presidential address to the Neurological Section of the Royal Society of Medicine, gave child psychiatrists an

* My own dog had been quite uninterested in himself until he was a year and a half old. I then noticed him paying friendly attention to my image in a long mirror, and he was bewildered when I addressed him from the object position. When put where he could also see his own image he reacted as to a strange dog in the room, standing his ground and barking the intruder off. I led him up to the "intruder" and he, finding that this animal had no smell, reacted with intense fear. Now at the age of four years he can wag his tail at the image in a very pleased way.

exciting contribution when he said that the function of the cerebral cortex is to give us a symbolic representation of our world. If we can rely on the E.E.G. at this age, my patient appeared to have started life with a general cortical abnormality. All that the brain knows must be taught by experience. The body image is built up of the summation of the impressions of the skin and muscle and position senses, collected from not only the clothes and the bed-clothes and active movements of the body, but from the fondling and the play by the mother ; the tracing, in love, of her child's features and form, by constant repetition, draws on the child's mind the image on which it bases its knowledge of life. This patient, as other schizophrenic patients, was handled little, its feeding was a bottle put to its mouth and emptied as mechanically efficiently as possible by a mother who had no time for extras. Its bathing was the matutinal removal of dirt as expeditiously as possible. Its image was never drawn. The most poignant scene of the Langley Porter film was the infant strapped into a high chair for its feeds when it could barely support its head. Its back had never been cupped perceptibly by the more supple arm of mother.

At six months the average child has collected enough perceptions to begin its simple additions to a composite whole. It has already added hand, eye and object together physically. Now it adds perceptions. The schizophrenic child is still having difficulty with its sensation-collecting, which is so poor that the child begins to show its discontent all the more enhanced because its special sense development has usually out-distanced its general sensation maturity. It appreciates the blackness of night visually without the reassurance of its body image. Life means nothing in the night and the child becomes fearful and fretful, even so terrified that it cannot be pacified until it can see again with its own eyes (like the little boy with the dog). This change is commonly seen in schizophrenic children who, until the age of five to seven months, may have been as good as my patient. It is interesting to note that speech, which is begun as a *sensuous* pleasure, was delayed and distorted in my patient. Creak and others remark on the frequency of the disturbance of speech even to mutism.

I am therefore postulating that schizophrenia in childhood is an arrest in the development of abstract thought and emotional maturity at an infant or toddler level ; that this arrest is dependent basically upon a defect in the aquisition of general sensation ; and this is due either to a defect in the neurological systems concerned with touch, pain, temperature, position and vibration senses or to faulty stimulation from outside or both ; and this defect leads to a delay in the formation of the body image and other images. On this hypothesis I can conceive a scheme of treatment which would be on the lines of remedial sensation development, involving mild massage, almost fondling, of the whole body daily, gymnastics, dancing, play in water, graduated from the passive to the active. All these activities would be modified to include all the physical sensations, contacts and play experienced by the normal infant and toddler. This physical approach would require to be linked later with remedial play to undo the fixed wrong ideas and attachments which have arisen out of the pathological thinking.

Unfortunately I have at my disposal no possibilities for experimenting on these lines, and I publish my hypothesis in the hope that a centre with adequate in-patient facilities may view it favourably enough to consider criticizing it from a practical point of view.

I wish to acknowledge my indebtedness to Dr. Szurek for permission to publish from his material, and to Mrs. Phyllis Preston for allowing me to use her astute observations of this child in the group.

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# DREAMS IN SAND.

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The inadequacy of verbal development is the most striking handicap to the analysis of children. In the young child, under seven years, many concepts such as "happy," "sad," and "worried" are frequently not recognized at all; the child's very vocabulary is too limited for expressive purposes. Even as late as pre-adolescence the child may fail to correlate its inner experiences with its vocabulary. Besides the limitation of vocabulary due to intellectual immaturity there is also the Super-Ego's restraining action on what may be expressed verbally, in cold blood, and the younger the child the greater is this restraint. Most children, however, given an adequate medium other than words, are richly expressive of themselves but, unfortunately, it is now the adult who is inadequate and frequently fails to understand the language that the child is using, or, understanding it, cannot express himself in it. He "interprets" for the child in the more adult language of words, and sometimes even at a more adult level of erotic and emotional development than the child's. When this happens the child usually demonstrates its inability to correlate the inner experience which it is expressing in its own language with the adult's verbal interpretation. It either takes no notice or is frankly puzzled, or gives up its expression as if stunned by the unexpected.

Many media have been tried to facilitate the analysis of children. Possibly the most favoured is paint. This is certainly of great use therapeutically if only through a general catharsis. The medium itself gives an erotic stimulation, especially if finger-painting is used, and various gross feelings can be expressed with satisfaction through certain colours (e.g., black and red) and by certain techniques (e.g., splashing and smearing). Unfortunately, painting to be successful in depicting concepts and conflicts requires a certain skill and, until the later years, children have not the proficiency to paint exactly what they wish to express. This inadequate expression leads to a feeling of frustration. Younger children tend to become stereotyped in their productions owing to the limitations of their abilities, executing the same type of house, landscape, flower pattern, "flag" without much evolution or progression or unfolding of material that would help in analysis. Moreover, the therapist, unless skilled in art, has to resort to a verbal communication with the child, for if he attempts to participate at the child's level he must perform with reasonable proficiency lest he disturb the child's expression. The child must be able to recognize that which the therapist intrudes, otherwise it is merely treated as an interference to be ignored or painted out.

The same criticism applies to all plastic media. As catharsis they may be excellent, but until the child has sufficient manipulative skill in that medium he is not able to express his concepts adequately to the therapist, and both this and the therapist's own limitations in the medium prevent the formation of the ideal bond between therapist and patient: it keeps the therapy at an empiric level and more in the hands of the patient, since the therapist cannot really control that which he does not fully understand.

The most therapeutically exciting and satisfying medium in my experience is the sand tray with its equipment. Here is plastic material in the shape of sand and water by means of which gross feelings can be expressed, for it can be thrown, tossed, moulded, plastered, dug and smoothed; and on this basis concrete symbols can be placed so that a situation is very easily presented to the gazer. The whole is capable of rapid change and evolution or of dissolution and destruction. The

medium is simple enough for adequate therapeutic interference and it is with ease that the therapists can discuss the situation in the child's language. The *forces* of the psychiatrist can be placed at the disposal of the child before the child's very eyes. (Until and even during adolescence it is often very necessary for the patient to have concrete proof of the bond between himself and the psychiatrist before he can benefit from therapy.) *Fences* and *barriers* can be pulled down gently, *wild animal feelings* liberated with impunity and *conflicts* resolved at a level satisfying to the emotional and erotic level of the child, and easily interpreted intellectually by both therapist and patient, for the position is plain for all to see.

When I applied the adjective " exciting " to this medium I meant that here, probably, is the most thrilling of all psychiatric experiences. For some time I have been struck by the dream appearance of the sand tray when viewed as a finished entity. In adult analysis the therapist listens to dreams and is involved by the patient in certain bonds and situations of a spiritual nature, tenuous and abstract, but in analysis of children, through the sand tray, the therapist can become part of the actual dream, moving in this subconscious world symbolized, contracted, elaborated, transposed, transfixed into the shapes, figures and schemes recognised as dream-work. At the dream level the psychiatrist can insert the exploratory finger, smooth over the roughness of a situation, heal the breach, cut the bonds, all non-verbally, as it were—" In the silence of the sleep-time, when you set your fancy free."

Children of all ages even through adolescence, once the *rapport* has been established, will drop quickly into this dream state. They become absorbed in the moulding and the fashioning of the sand as if in the process of falling asleep. The shaping seems to be analogous to the tracing on the wall and ceiling of the hypnagogic patterns that are the entry into the unconscious state of the dream world at night. This fashioning may remain basically the same for the specific child ; a smooth, slightly concave base remained throughout the formations of a child of five ; a boy of seven related everything to a tall central structure surrounded by a deep and furrowed moat ; a girl of eleven preferred a flatness with a rough surface. On this basic personal structure moves the play of those matters troubling the child. Words need not be omitted entirely. As in dreams, where usually the expression is in mime, verbalization and even vocalization does occur, and where the bond between therapist and patient is strong the psychiatrist can utter the scream of terror, the wail of sorrow, the cry of hate, the " How vile!" and the " What a dreadful thing!" that will not come from the child's dumb mouth that by this sympathetic encouragement the child may be helped to a better catharsis.

The extraordinary phenomenon of this dreamlike state is its serial nature. More and more rapidly at each interview the child will make the personal foundation which will show some modification as the child progresses. Parts of situations may be repeated and recalled from former interviews, and from this stage the statement in symbol will continue. To facilitate the process it is essential that the constituents of this sand-tray language should be arranged in an orderly dictionary (as it were), so that the child does not have to waste time looking for the representation of the words " mother," " house," " bondage," " conflict," but the feelings may flow freely and the dream progress rapidly because the symbols are at hand and in the expected place. Unless this equipment is arranged on easily accessible shelves in a standard order to which it is returned before each session, the child can only express itself stammeringly and haltingly. If presented with this facile, organized language, children of all ages will unfold their inner selves in a fascinating way impossible in any other medium.

Adolescents may require an explanation of this language to overcome their intellectual barriers, but I have used this method with remarkably rich results in fifteen- and sixteen-year old girls and boys. Even where full verbalization is intellectually possible the method remains the most therapeutically satisfying because of the union between psychiatrist and child in person at the dream level. I had pandered to the intellectual development of a girl of fifteen using painting and verbal techniques without success. She still remained enuretic, and kept herself and her conflicts away from me. We knew that the girls' mother had treated her disgracefully, but the girl refused to face the reality of her emotional state and the attitudes resulting from that treatment. Finally I took her to the language of the sand tray, to the concrete dream level, and in a series of six sessions she had expressed her " awfulness."

All the other animals in the world were on the pleasant hills under the trees, shaded from too hot sun and safe from danger. They were united into families, but in the unsafe patch, in the middle of the morass, were two calves, brother and sister, whose mother had left them and was herself on the pleasant side of the world.

This statement evolved into more human expressions of the unhappy situation until the last was obvious in relationship even to the child, and she was able to express with grief and horror the reality to which the dream had been so near.

A farmer and his wife lived on the most prominent hill with their son, a boy of the same age as the patient's brother, who was more accepted by her mother. Everything was at home and safe but the farmer's wife had not bothered about the last of her chickens, who was trying to get across the stream and reach home before the wolf ate it. The chicken was very frightened, but felt that perhaps it would be alright because there was a friendly bull (coming from the therapist!) who would fight the wolf and save the chicken.

Together we were able to say what a terrible person was the farmer's wife—and the child's mother. With this release of aggression against the mother the girl's enuresis cleared. Throughout, the basic sand formation had been a pattern of hill at the periphery with a central morass later turning to a definite stream.

The dream-like evolution of the sand tray picture is shown excellently by the series of photographs of the formations made by one boy of thirteen years. The series is far from unique in my collection except that in this case I was able to obtain photographs instead of the sketches that I usually keep for record purposes. The lad's clinical story is not of importance save that he was of psychopathic inheritance, knew nothing of his parents, imagined that his father was in America, had suffered much from mother-deprivation, had grown no roots for he had been moved from home to home, and was of that inadequate psychopathic structure that can exist socially only with obsessive bonds. He had high aspirations and low morale, and had broken down at the onset of adolescence with a depressive condition manifesting itself in stealing.

Throughout the series the patient worked from the left of the picture while I sat on the right. We faced each other. The part of the tray termed " Background " stood against the wall. The tray could only be seen as a whole from the " Foreground " which is the front of each photograph.

*Formation I.*

The foreground was constructed first. A house with two chimneys and an adjacent coal cellar (not visible in the photograph) stood inside its own grounds which were fenced off from the rest of the world. In one corner was a summer-house almost as big as the main house, the winter house, which the patient preferred because it was warm inside. Although warmth was sometimes needed in the summer-house because of the cold atmosphere around, fires could not be lit because there were no chimneys.* One part of the garden was raised into a small kind of island. The back-ground remained a sand wilderness, and the patient agreed with all his heart that it looked very lonely. I shuddered and said that I thought I might be frightened to be in such a lonely spot. He began to smooth the sand upwards to make a mound in his own corner and he propped a motor cycle against the summer house on which to go away.

The wilderness took shape rapidly after this. A castle appeared near the patient, and behind it, more in the background, was a structure with a hole in it leading to an underground railway. A main road from him to me was smoothed out, and from it led a secondary road to the underground railway. All the traffic along the main road led from him to me except the milk-van, which came from me delivering milk to all the buildings. My position he designated the Sea.

An imposing house with many steps leading up to it came up on my side of the background. This was the Lord Mayor's Palace. Outside this, on the secondary road, the patient placed a sign which he had wanted to be HALT! MAJOR ROAD AHEAD, but unfortunately this was missing from the set and a substitute was used. Outside the castle should have been a notice pointing to the Railway. The policeman was holding up the traffic from the railway, a horse and cart—slow traffic compared with the vehicles that flew along the main road from him to me.

He could not verbalize beyond the identification and saying that the houses were where rich people lived and that there was a connection between them. Yet he had

* This boy had become depressed first in May and had grown worse in August.

said more plainly than any adult in a first interview that although in the main there was good communication between us, there was a double censorship holding up the flow from what lay underneath, the more powerful unconscious. I had been passive except for a rare comment.

*Formation II*, 3 days later.

He made this with exquisite and loving care. At his suggestion I altered the HALT sign to TO THE CROSS ROADS while he made the foreground. He finished four mounds, with three signs placed as in the photograph and a cross of roads and presented it to me with " There!"

I remarked on the deadness of the picture and that I could see nothing happening. I supposed that it was night time, but he corrected me for it was day-time and he fashioned the structures more clearly, adding an island at the cross roads and putting in the wooden figures.

Here is basically the same structure as in Formation I. The winter- and summer-houses have disappeared into a road that leads slowly to the main road ahead. The front fence of the garden has vanished and the raised piece of garden has moved out to become an island in the main road at the junction of the original road to the Underground and the road that was the houses. Both side hedges remained as structures but they were now modified to two rows of houses, ordinary houses where ordinary people lived and their front gardens, abutting on the road, were on the original garden site. The mound at the patient's side had melted into little mounds which were the walls of the back gardens beside him.

The most interesting mutation is in the background where the structures, still in the same position as in Formation I, are now almost of equal size and similar in shape except that the centre of the right hand is raised while that of the left is depressed. That which had been a Castle was now a big Cinema with " lots of pictures " and some buried treasure (his stick with which he had fashioned the chimney stacks). That which had been the Lord Mayor's Palace had been converted into luxury flats by an American with lots of money who had come over here and bought up the palace. The patient emphasized that he would never go there for it was too " posh."

My position was still the Sea and still milk went from me to all the buildings. The main road traffic continued to pass from him to me. The policeman and the instruction HALT! had both gone for ever. The latter had been replaced by the sign TO THE CROSS ROADS.

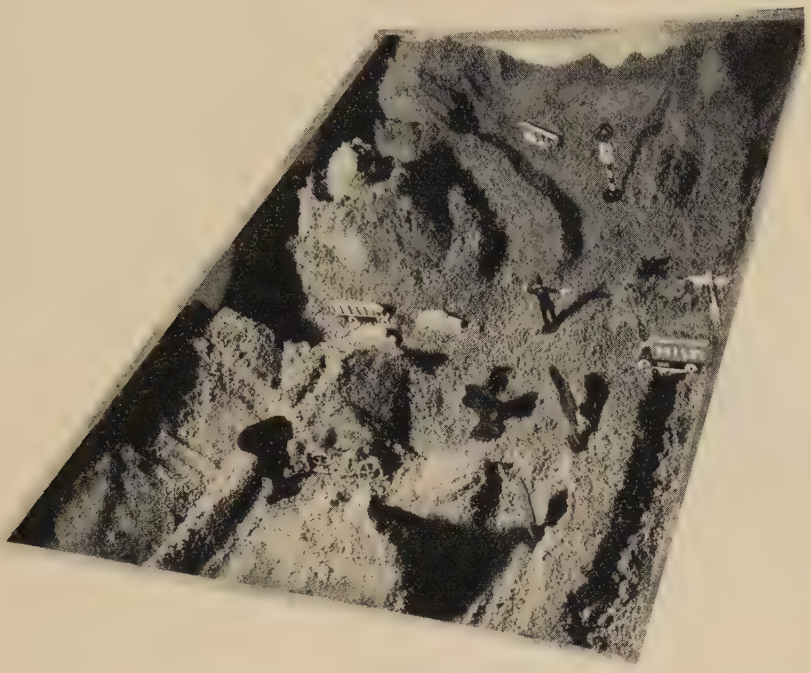
*Formation III*, 5 days later.

He referred to his last formation and said that he would not like to be "posh" but would rather be in the little houses, so identifying himself with the foreground of both formations. He told me that everyone on the formation went to the Cinema, rich and poor, but the posh people from the luxury flats went upstairs in the " Gods."

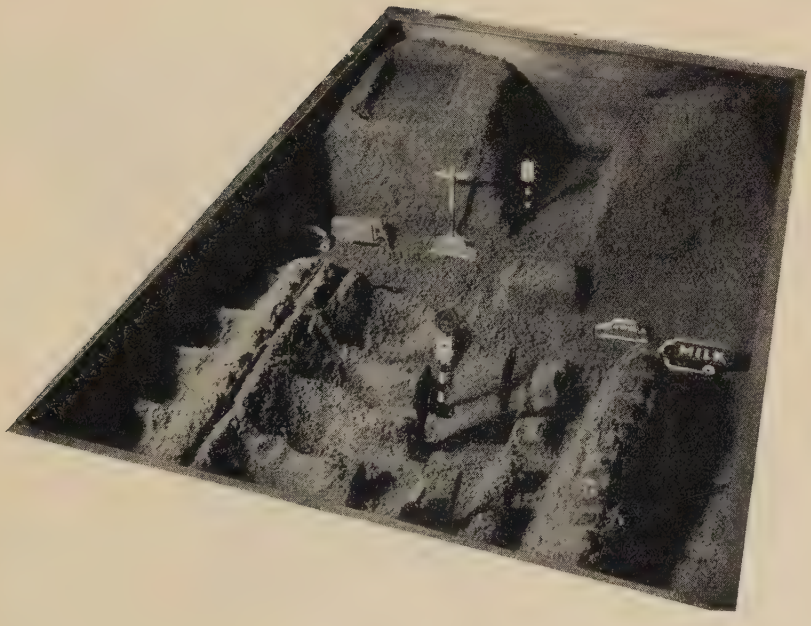
As he spoke he drew an island in the sand, scratched out a box-like hole and covered it in again. This has been a sudden feeling of a grave. I wondered aloud whose it was, but taking no notice of my query, he began an extensive formation in which he continued to look for his lost stick, although he kept overlooking it, burying it again whenever it turned up. He left his side and came round to lay at my feet a pile of sand, the surplus from his smoothing process. Then he dragged me into the dream play with " Guess what this is!"

*Therapist :* A castle? A football ground? A race course?
*Patient :* A race course. Hounds. It's at night.
*Therapist :* Can't we have a race? We have dogs here. And where are the people?
*Patient :* Oh, usually they stand there and pay money to go in. But it's night and there's only you and me.
*Therapist :* A race just for us! How lovely! Didn't we have to pay?
*Patient :* No.
*Therapist :* How nice! We must be special people.
*Patient :* Oh no. Anyone can go.
*Therapist :* Wouldn't it spoil it if everyone got in free? Nobody would pay if they could get in free and everyone would come and the place be overcrowded.
*Patient :* Only we knew about it.
*Therapist :* Then we must be special.
*Patient :* No! No! The man who owned it sent a boy to advertise it but he didn't. He just told us.
*Therapist :* Then when the man gets to know he'll sack the boy and get someone else to advertise and then everyone will come.
*Patient :* No! Because he wants to keep the boy. So we'll be the only ones there.
*Therapist :* In other words, you want us to be special but you don't like calling us special.

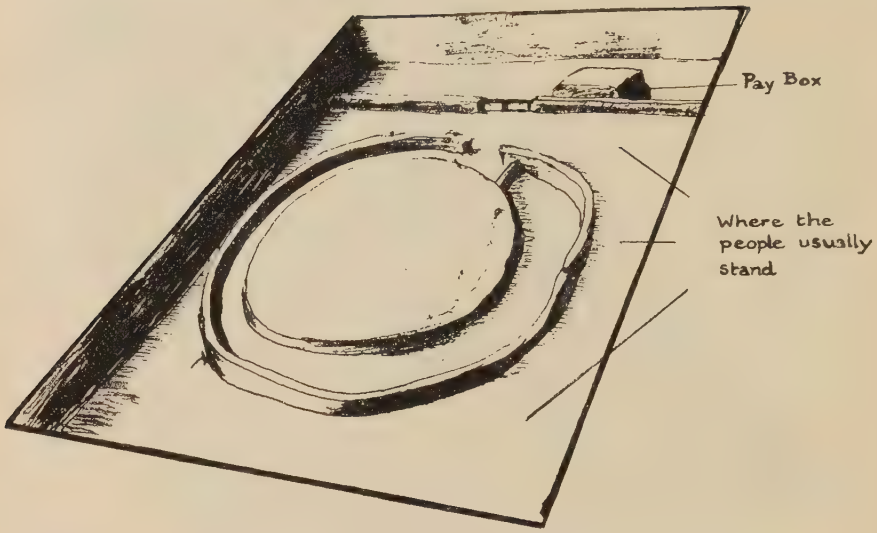
Patient laughed and the dream play almost ended as if the Censor had awakened to the imminence of reality. I said, " How nice it would be if we two could have something



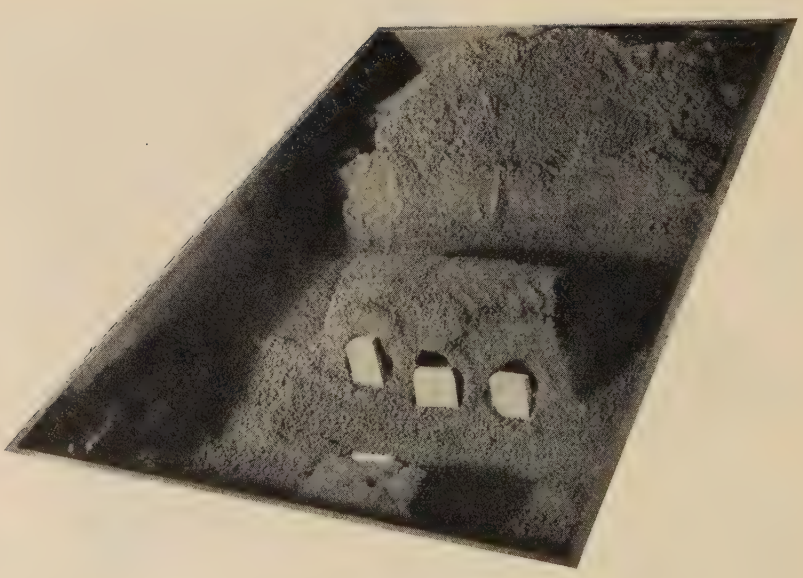
FORMATION I.




FORMATION II.




FORMATION III.



FORMATION IV.

together and free, a race all to ourselves at night. It's very nice of you to want me with you. I wonder which dog wins, yours or mine." He ran a race very carefully and made our two dogs finish first, in a tie. The others had left the course.

He scrubbed out this formation and I can therefore only present my drawing. The formation was obviously a development of a specific part of the first two, but whether of the Island, which had come from his garden, or of the Castle which had mutated into the Cinema it is difficult to say. Most probably this is an example of condensation. The Castle and the Island have fused. Note that there is a remnant of the Flats or Super-ego corner, the Pay Box, which is barred off from the rest of the theme.

When I expressed regret that he had destroyed this (My secret zeal for photography having outrun temporarily my therapeutic sense) he made another scene, *Formation IV*, which had an unidentified mound spreading from the Flats area, a mound of greyhound kennels in the Main Street area, and a separate house for our dogs in the foreground, his own area. Everything was " shut up for the night." I think that this demonstrates very plainly the uselessness of trying to force the analytical process. This was emphasized by the next interview, three days later, when the patient dug holes in the sand and filled them in again in a very dissatisfied way.

*Formation V*, 1 week after Formations III and IV.

He traced on the sand, in quick succession, something of his rows of houses, the island and the dog track before he burst into the making of Formation V. Once more he came round to me in a dreamlike way to put sand at my feet as he, so deeply absorbed as to be almost in a state of altered consciousness, fashioned with exquisite care the dream picture. Once more we had a cross of ways but the Main Road from me to him was the firmer and passed over the fluid way that had evolved from the connection between himself and the Underground. Once more there were two main mounds in the background ; that which had been the Castle and the Cinema was now pleasant country and was bigger than the other mound which had passed from the palace to "posh" Flats, a Pay Box and now into a penned field containing a lonely ram. Pleasure boats sailed along the river. The car on the bridge was taking the patient and myself home from a day at the sea.

*Formation VI*, 10 days later due to a holiday intervening.

(This picture I hesitated to include for it appeared to be the beginning of a new series. Unfortunately this lad's treatment was administratively interrupted here and I have no further records for comparison.)

Blocking my view was a house meant to be the hospital part of the Home from which he had been moved recently as it was felt that his suicidal tendencies had subsided. He asked me to help by making the roof of the verandah for him and, as a wide road led from me to the front door under this verandah that I had made, and as the window jutting above it was the matron's room, I felt that I was correlated with the matron.

Behind this house, fashioned out of my sight (although I was given my customary present of sand out of the excavations), were steps leading up to the back door which the patient preferred, and also steps leading down to a place where dustbins were kept. The steps led up to " where we play," indicated in that corner where the Castle, Cinema and Country structures had been. The foreground, which the patient called " the Side " was not in the picture. The mound which had been the Super Ego structures was unformed. It was night.

It is possible that in this picture the Castle-complex had been displaced into the centre of the picture, for the pathway to the underground hole of the dustbins was reminiscent of the road to the Underground Railway which was under the square structure at the *back* of the Castle in Formation I. I should not like to draw definite conclusions for the purposes of this paper without examining this formation in relation to the rest of the series which was never obtained. Later he sent me a very inadequate drawing which he called the inside of a machine, " the Mole," which could go underground, and this might be taken as corroborative evidence for my assumption about the last formation.

The analysis of this material I do not wish to attempt here although much of it is so obvious that one scarcely needs psychological knowledge for interpretation. I only wish to demonstrate that these formations " are such stuff as dreams are made on." Here, before our very eyes, are the symbolic acts—the laying of dirt at the feet of the vast mother figure not actually seen in the dream picture ; here is the dramatization whereby the latent idea in the content is turned into action ; here are the condensations of several aspects into one symbol which mutates before our eyes to give better expression to the individual facets without change of basic feeling structure. So the Lord Mayor's Palace was bought by a rich American and converted into a " posh " place above the aspirations of the dreamer, a place where lived people who went in the " Gods," a place that constricted to a Pay Box and lastly expanded into a field of restriction where dwelt a solitary ram. It

FORMATION V.

FORMATION VI.

remained a masculine Super Ego place on the doctor's side. It remained raised, altered its shape but little and its position not at all in the series that was obtained. So too, the Castle, a place for defence and refuge, became the place for pleasure, the Cinema, and then a place of freedom and relief, the Country. Even when the complex moved to the centre for discussion its original site retained the flavour of freedom and recreation. As in the dream, two completely separate figures can be compounded into one, and latent elements sharing common characteristics are blended into a single whole. In Formation III it was difficult to know whether the racecourse was an elaboration of the Castle or of the Island for it was reminiscent of both. As in the dream the centre of interest can shift, only in the sand the separate complexes are shifted in turn to the centre instead of the centre shifting. From what had gone before it seemed only a question of time before the very difficult Super Ego complex would be moved from its corner to the centre for discussion. Freud points out that the essence of the dream function is regressive, as it implies a translation of the wish into an archaic form of language, and surely the most archaic of all expression is the concrete representation as we can have in the sand tray.

A form of secondary elaboration is obvious in connection with all the formations and the same incongruities are found as in dreams—the rich people go in the " gods," milk was generated at the sea, a structure is heightened to become flats—but probably this is more obvious in Formation III where we return to verbalization. There was here a considerable degree of rationalization. Because the latent elements have been replaced by something more remote, by an illusion as it were, the formations have too that same remote intimacy which is the quality of those vivid dream pictures that our censors allow us to recall or which press beyond our censors because of their intensity.

In the normal person the dream life is sufficient to satisfy the forbidden desires and enough catharsis to heal the wounds of the day. Sleep " knits up the ravelled sleeve of care " completely each night. There is no need to examine and discuss these dreams or to analyse their contents. So in this therapeutic dream work where the therapist and patient converse in symbolic language I have found little need for interpreting to the patient verbally. I sometimes assist catharsis by sympathetically expressing vocally the emotional trend of the dream, often in exclamatory form, and this, together with the patient's satisfaction of expressing perfectly in this displaced way the forbidden wishes, desires and fears, has proved therapeutically valuable. Children improve rapidly, as did this boy until his treatment was interrupted at this crucial stage in his analysis. This freedom from the need for verbalization is an immense relief, for even for the skilled therapist it is difficult to translate adult interpretations into the exact level of concrete or abstract thought development, erotic stage and emotional maturity at which the particular patient may be. The archaic language of the sand tray reduces all to a common level. Moreover we know that, therapeutically, deeper satisfaction is obtained from feeling and doing than from thinking and saying.

The basic structure of flatness remained specific to this boy in all the formations and I have noted this basic tendency in formations made by children over seven years of age. At a younger age the bases may be less defined. It is possible that by analysis of these basic patterns and their origin we could find clues to the basic personality structure of the patient and evidence of the progress of personality integration. At the moment, however, I am impressed by the depiction that the moulding of the conflict and superficial material is dependent upon the shape and structure of the basic formation even as any clinical picture is coloured by the underlying personality. I should like to urge greater interest in and analysis of this sand-tray medium and its possibilities that we may learn more of the associative processes and their formation, of the dream mechanisms and therefore of the thought, feeling and erotisms in the child, and of the analysis of children generally.

# AN ATTEMPTED CORRELATION BETWEEN CLINICAL AND PSYCHOMETRIC FINDINGS IN SENILE-ARTERIO-SCLEROTIC DEMENTIA.*

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## Introduction.

Recent research from psychological, psychiatric and social viewpoints has emphasized the importance to the whole community of the aged population, and has stressed in particular that the changing proportion of aged to working populations is bringing with it problems of great urgency.

This has been noted by Sheldon (20), and other statistical surveys carried out in America (22,18,16) reveal that the problems facing an ageing population are no less urgent there. The realization of these problems has stimulated a growing body of research on the older age-groups with the object of promoting as full a knowledge as possible of the mental and physical capabilities of this section of the community.

## Earlier Work and its Principles.

The work of Wechsler (23, 24), Miles and Miles (17), Jones and Conrad (14), Foulds and Raven (9) and others has established the decline of intellectual abilities with advancing age. This would seem to be a differential decline for various abilities, a maximum deterioration being found in abstract reasoning ability as opposed to verbal ability which holds up relatively well. Cattell (5) distinguishes these two types of abilities as " fluid " and " crystallized " ; the former has the " characteristic of a purely general ability to discriminate and perceive relations between any fundaments, new or old," the latter consists of " habits long established in a particular field, originally through fluid ability, but no longer requiring insightful perception for their successful operation."

Babcock (2) and Shipley (21) have independently used this principle of differential decline in their tests for mental deterioration. Both these tests, however, in their assessment of fluid ability depend on previously acquired knowledge in the form of verbal or arithmetical symbols.

On the basis of these principles the abilities of the senile age-group have been assessed by M. D. Eysenck (7). She applied a series of 20 tests, including the Board Form of Progressive Matrices (Sets A and B) and the Mill Hill Vocabulary Scale, to an unselected group of 84 patients with senile dementia. The results were factorially analysed, and she concluded that the mental ability of the subjects had deteriorated considerably. Deterioration had affected fluid abilities most and crystallized abilities least ; the organization of these abilities as compared with normal adults had become profoundly altered. An analysis of the errors made by the same group of seniles on the Progressive Matrices test (8) showed that there was no significant disparity between their types of error and those made by normal adults and normal children with whom they were compared. It would appear, therefore, from this study that such differences as do occur between seniles and normals are *quantitative only*.

No absolute deterioration quotient was given by this investigator, but the average mental age of seniles on Progressive Matrices is 8 years, and on Mill Hill Vocabulary is 14 years.

A comparable investigation, using a battery of 25 tests, including Vocabulary

* Abstract of paper read to Annual General Meeting of R.M.P.A. at Crichton Royal, July, 1951.

but omitting the Progressive Matrices, was undertaken by Halstead (11, 12) on a group of 38 cases of senile dementia. Eighteen of this group were in a more advanced state of deterioration than the remaining 20 with whom they were compared. He concluded that the tests did discriminate between the two sub-groups, and suggests that it is necessary to explore various facets of intellectual ability in order to construct a fully comprehensive picture of the deterioration present. Nevertheless he finds that the individual test profiles thus obtained differ so widely within the group as to *preclude any convincing correlation with clinical data.*

The first of these investigations indicates the difficulty of validly assessing mental deterioration in this age-group. The basic assumption of the Babcock and Shipley techniques is no longer tenable, and deterioration is given as a *relative* fall between vocabulary and matrix scores. Also, it is given in terms of group means which will mask many discrepancies in individual scores. The second investigation finds difficulty in correlating psychometric and clinical data, and points out a wide range of differential deterioration in different abilities. The author mentions the value of a qualitative analysis of the results, although he does not undertake such an analysis.

Brody (3, 4) also made reference to the value of a qualitative analysis, in the course of evaluating his results in 83 hospitalized cases of dementia, more than half within the senile age-group. Using, among others, the Babcock test and Terman Merrill Vocabulary Scale, he confirmed the disparity between scores on fluid and crystallized abilities, and devised a novel method of presenting the difference as a discrepancy score, which gives a measure of the degree of dementia. His conclusions, after a qualitative survey of the results from the same group, are that (1) " dementia affects patients in inverse proportion to the pre-psychotic ability." (2) " Some vocabulary deterioration occurs earlier in dementia than has hitherto been supposed and in the absence of clinical signs thereof." In other words, in his first paper he accepted the basic assumption underlying the Babcock technique for measuring deterioration, and in his second he found that it is not tenable. The trend in these investigations is, therefore, to doubt the stability of vocabulary scores with advancing age and dementia, and to substantiate this doubt by a qualitative analysis which demonstrates the deterioration in vocabulary when clinical and purely psychometric techniques fail to show it.

Further evidence comes from Yacorzynski (25), who thinks that vocabulary level is apparently maintained into late maturity because of the wide range of acceptable definitions for words. If the method of scoring were to take into account the quality of definitions given, the end-result obtained might well be significantly altered. Using the routine method, the quantitative score is unaffected by definition level, whereas in fact mental deterioration may well have eliminated the more abstract meanings.

At the same time, Cleveland and Dysinger (6) studied a small group of 20 institutionalized patients by comparing their performance on the Object Sorting test of Goldstein and Scheerer (10) with their results on the Wechsler Bellevue Scale. They found a marked discrepancy between the subjects' level of performance in sorting objects (which was largely by concrete criteria with loss of the conceptual or abstract principle) and their performance on the verbal items of the Wechsler Bellevue Scale, where the responses were apparently on an abstract level. The authors explain this apparent discrepancy in terms of Goldstein's hypothesis (10) that the ambiguities and uncertainties inherent in the meanings of words allow such patients to mask their actual loss of the ability to abstract by their facility in the use of words. Thus they remain capable of verbal responses which apparently indicate their continued recognition of conceptual relationships, while in fact such recognition is actually beyond their capacity when faced with an objective situation as in the Sorting test. In such a situation the loss of the abstract attitude can be seen in the patients' inability to perceive and define objects in other than strictly utilitarian terms, ignoring abstract characteristics. This finding was suggested much earlier by Hirsch (13) in his descriptions of the performance of deteriorated senile patients.

Even more unequivocal in the confirmation of vocabulary deterioration are the conclusions of Ackelsberg (1), based on her investigation of 50 institutionalized cases of senile dementia whose performance she studied on a group of five tests designed to assess various facets of the knowledge of word-meaning and usage.

The tests used were synonyms and antonyms, determining the patients' ability to perceive relationships between words and so differentiate between similarities and opposites; a word categorization test to ascertain the subjects' ability to classify several "species" words when linked with a common "genus" word; a word-naming test to estimate the patients' fluency in a given time and; finally a test in which the subjects were required to list as many different meanings as possible for each of a set of 12 words, each of which has several meanings. Her statistical and qualitative analysis shows that verbal ability does decline with dementia.

From the foregoing review of literature on this subject a number of points emerge as worthy of note:

(1) There are good grounds for supposing that vocabulary is affected by deterioration.

(2) The deterioration of vocabulary can easily be missed if only quantitative results are taken. The importance of qualitative assessment for tests other than vocabulary tests has also received emphasis by many authors.

(3) The senile age-group presents peculiar difficulties in psychological testing. These have been summarized by Jones and Kaplan (15) as (*a*) the lack of readiness to co-operate in tests; (*b*) wide variation in performance due to the stage of advancement of the illness and the length of hospitalization; (*c*) differences in the original mental endowment, which is known to be a factor in the rate of intellectual decline and which, therefore, affects the test scores; (*d*) differences due to the effects of background, general interests, educational status and general environmental influences; (*e*) factors of poor physical health, increased fatigability, emotional lability, impairment of attention, concentration and memory which are so characteristic of senile patients.

(4) There is a wide range of ability in the normal senile age-group. With the added complication of psychosis it is apparent that considerable care is necessary in selecting patients for a test group, and adequate clinical data must be fully used.

(5) The application of batteries of tests, standardized on normals or on a young population, can be very misleading.

(6) The interpretation of results in terms of group means is of little value unless the difficulties noted above are taken into account.

## Aim of the Present Study.

Although the value of a qualitative assessment of results has been noted in not a few investigations, it has been neglected or limited to a general descriptive level which, while valuable, does not link up adequately with the quantitative results. The present study tries to combine both quantitative and qualitative approaches.

The aim is to provide a sufficiently comprehensive assessment of senile intellectual performance as to evaluate not only the level of intellectual deterioration but the degree of emotional adjustment to that deterioration, and to compare the methods of solving used by seniles and children.

### *Population Tested.*

The group used for this investigation was drawn from the age-group 65+ among the Crichton Royal Hospital patients. This totalled 330, but only those diagnosed as senile dementia or cerebral arteriosclerotic dementia were taken, with no history of a previous psychotic attack. Also excluded were patients suffering from aphasia, deafness, paralysis, blindness, etc., to a degree likely to make co-operation in the tests difficult. Fifty patients were found to satisfy these conditions. Ten, however, were so seriously demented that they were unable to grasp the nature of the task; the remaining 40 were tested.

The mean time in hospital and the mean duration of illness proved of little value, and no valid conclusions can be drawn from them because of the very wide scatter, and the extreme difficulty of finding accurate figures for the duration of illness. The *range* (in months) for time in hospital extended from 1–72, while duration of illness varied from 1–156.

The patients were graded clinically into five groups, A to E, E being the most demented. No correlation was found between clinical grading and age. The mean age of group E is the same as that for group B, with the intermediate grades having a lower figure. There also appears to be no sex differences correlating with age or degree of dementia. The age range was from 60–90 years, with a mean of $74{\cdot}8 \pm 7{\cdot}8$.

*Tests Used.*

The Progressive Matrices Board Form (1947) sets (19a, 19b) A, Ab, B was used for the assessment of current intellectual output. This test was specially designed for use with children (age 3–10), and those who, for some reason, are mentally impaired or deteriorated. The three-dimensional form overcomes the difficulties of seniles in dealing with spatial relation problems presented as printed diagrams, while the insertion of the Ab set, intermediate in difficulty between A7 and B7, gives a wider range of problems within the grasp of this group. The test has not been standardized for the senile group and tentative children's norms are used. The test has the advantage that it is independent of previously acquired knowledge or symbols and the instructions can be grasped with a minimum of speech.

Previously acquired knowledge was tested by the Mill Hill Vocabulary test, norms being available from 5 to about 60 years.

No time limit was imposed, and these tests only were used because of the difficulty of holding the attention of seniles for any considerable length of time. The testing session ranged from one to three hours, but there were many interruptions due to patients tiring, becoming talkative about irrelevancies and frequently requiring expediencies for motivation. Actual testing time was rarely more than 30 minutes.

In the Progressive Matrices test the patients were encouraged to talk about their method of solving. This verbalization of method gave valuable information for the qualitative analysis and helped to eliminate chance correct responses. In some cases, however, the patients were unable to give clear accounts of their methods.

*Reliability.*

Both tests were repeated within 6–8 weeks, but only 32 of the original 40 could be re-tested. Five had been discharged, two had died, and one, a paranoid state, refused to repeat the test. Instead of the Pearson-Bravais re-test correlation, therefore, the Kudor-Richardson test of internal consistency was used. The reliability coefficients were 0·77 for the Progressive Matrices test and 0·9 for the Mill Hill Vocabulary test. The means and standard deviations were: Progressive Matrices 21·05, 5·85, Mill Hill Vocabulary 43·65, 16·5.

In the Mill Hill Vocabulary there is a much wider range of scores ($\sigma = 16{\cdot}5$), representing a mental age range of $7\frac{1}{2}$ to normal adult, say 50 years. This is probably due to the wide range of acceptable definitions, all of which receive equal credit. According to Yacorzynski it is because of this range of acceptable definitions that the vocabulary scores show less tendency to fall with age. Deterioration may eliminate more difficult or more abstract definitions without affecting the total score.

Accordingly, a system of qualitative scoring of vocabulary was attempted, but although a number of systems were tried, they all proved impracticable without modification of the existing test framework. Further research is being conducted with a view to overcoming this difficulty, but in the present study the qualitative approach to vocabulary had to be abandoned. Since the quantitative scores were considered of doubtful validity, it was not possible to arrive at an index of deterioration by the method hitherto used, and the method described here therefore depends on the patients' performance on Progressive Matrices.

## Methods and Results.

On the basis of independent clinical assessment the cases were divided into five groups, according to the degree of dementia. We then compared the quantitative scores of these groups on Progressive Matrices with the qualitative scores, as determined by the level of abstract problem correctly solved as described below. Statistical treatment showed that the difference between the means of each of these groups is significant, using the qualitative method, whereas similar grouping according to quantitative scoring gives a significant difference only between the best and the worst groups.

The quantitative determination of absolute deterioration thus appears to be an insoluble problem. This paper is an attempt, with the aid of a qualitative analysis, to put in quantitative terms the emotional reactions to deterioration, i.e., to estimate not only the degree of deterioration, but also the reaction to that deterioration.

*Qualitative Analysis.*

Our aim was to devise a formula which would tell us something about the patient's conception of the problems presented to him; his emotional reaction to these problems, and his method of arriving at a solution irrespective of the ultimate score in terms of right and wrong answers.

The first step was to list the 36 problems of the Progressive Matrices test in order of their degree of difficulty as found in our series of patients. Examination of this list showed that the problems could be grouped into various categories according to the type of Matrix. We distinguished in all eight sub-groups in increasing order of difficulty as follows:

(1) The simplest group consisting of the first five problems in the test in which the Matrix is an overall pattern with no superimposed complexity. We called this the *Overall Pattern Type* (Set A 1–5), and found that 94 per cent. of our cases solved them correctly.

(2) A group of problems in which the Matrix consists of three identical discrete elements requiring a fourth identical element to complete the pattern. This type was labelled *Simple Repetition of Discrete Elements* (Set Ab 1, 2, 3—Set B1,2), and was successfully solved by 76 per cent. of our cases.

(3) A third group of three problems (Set A 6, 7, 8), in which the basic overall pattern is complicated by the addition of parallel lines, the continuity of which is interrupted by the missing section of the Matrix. The completion of the Matrix depends upon the principle of linear continuity being grasped, and this type of problem is, therefore, called *Linear Continuity Pattern*, which was successfully solved by 61 per cent. of the patients.

(4) A fourth group of eight problems of the discrete element type but in which the individual elements, although still identical in other respects, are now so positioned relative to one another that the addition of the missing fourth element successfully completes a uniform pattern of configuration. To give the correct response to such a problem the patient was required to grasp the internal orientation of the individual elements one to the other so as to form a configurational entity. The label we applied to this type of problem was *Configurational Pattern*, and we found that the eight Matrices of this type fell into two groups, each of four, the easier solved by 55 per cent. of the cases (Set Ab 4, Ab 7, B 3, B 4), and the more difficult solved by only 40 per cent. of the cases (Ab 5, 9, 10, 11).

(5) A fifth and small group of two problems (A 9 and 10) conforming to the Linear Continuity Pattern but in which the lines are now all of varying width within the pattern. This type of Matrix is more difficult to solve because the patient requires to utilize two independent factors, namely linear continuity and varying width of line, to find the correct section. As opposed to the percentage of 61 who successfully solved the patterns of linear continuity alone, only 44 per cent. were successful with this type, which we called *Linear Continuity* plus *Varying Width Patterns*.

(6) A sixth and similarly small group of two problems (B 6 and 7) essentially of the Configurational Pattern Type, but in which the additional complexity of contrast in shading between the two halves of the pattern has been introduced. This contrast relationship must now be grasped in addition to the internal orientation of the discrete elements before the problem can be correctly solved. Thirty-six per cent. were successful with this type, which we named *Configurational Contrast Patterns*.

(7) A seventh group of three problems (Ab 6, Ab 8, B 5), again basically configurational, but in which the pattern is asymmetrical. Superficially the figure suggests a commonplace gestalt, identification with which breaks down, however, in face of asymmetry. The necessity for differentiating between affinity to a gestalt on the one hand and the fact that there is asymmetry on the other hand made this type of problem peculiarly difficult for our patients. Only 22 per cent. were successful in completing the Matrix. We called these problems simply *Gestalt Patterns*.

(8) A final group of eight problems, the most difficult of all, in which the completion of the Matrix is not facilitated by the structural characteristics of the pattern and in which the solution can only be gained through a process of *eduction*. In two of these problems (A 11 and 12) some contribution to the completion of the pattern may be made by the factor of Linear Continuity. We have, accordingly,

called these two problems *Eduction with Linear Continuity*, and 17 per cent. of our cases found the correct solution as opposed to only 10·8 per cent. in the remaining six problems, which were known simply as *Pure Eduction Problems* (Ab 12, B 8–12).

Having thus grouped the 36 problems into these eight categories, we now allocated a numerical value to each sub-group relative to its position on our index of difficulty, e.g., since the eduction problems were found by our patients to be approximately six times as difficult as the problems involving purely overall pattern, or simple repetition of discrete elements, the latter were rated as value 1, and the former as value 6, with the other types of problem proportionately weighted between these two extremes.

Complementary to this analysis and weighting of the Matrix problems, it was necessary to examine the various possible responses to each problem, and to allocate a rating to each type of response based on its degree of relevancy to the correct solution. In this the patient's comments on his method of approach to the problem proved of value. An example illustrates this procedure :

In Matrix A 10 the problem presents two complexities, namely, linear continuity and varying width of line. The patients who were capable of perceiving both these factors simultaneously and of co-ordinating them to give the correct answer were allocated the full score for this type of problem. A number of cases, however, were capable of perceiving only one of the factors involved. They made their selection on the basis of linear continuity, in which case they chose No. 1, or on the basis of varying width of line, in which case they selected No. 6 or, less commonly, No. 4. Both these responses bear some relevancy to the Matrix, but since the patient could only perceive one factor of complexity he was scored at that level for his answer, i.e., he was credited only with the value of the preceding type of problem, which in this instance was the Linear Continuity Pattern. If the patient failed to grasp the nature of the problem at all he chose either a completely irrelevant response, e.g., No. 5, or he inadvertently selected the correct answer which his verbalization showed to be a purely random choice. In either case he failed to score any marks for his answer.

Qualitative marking on these lines gives more detailed and more accurate information about the patient's performance, which may be analysed as follows :

1. Score up to the level of difficulty where the patient fails to solve correctly.
2. The first three groups of Matrices (13 in all) can be regarded as capable of solution on a concrete level, while the remainder require the ability to abstract in the sense described by Goldstein. The percentage score in the latter will represent the degree of loss of the ability to abstract and, therefore, give a measure of deterioration.
3. Score beyond the level of difficulty at which the patient solves correctly. In attempting problems which are beyond his capacity a patient may use the experience gained in earlier problems and choose a response which, while incorrect, shows some insight into the problem, or he may choose a response which is completely irrelevant. In the first case he was allocated marks appropriate to his level of solution, in the second he was marked zero.

1. The group was now divided into five sub-groups according to the level of problem passed, giving five stages of dementia. Compared with the clinical assessment there are nine changes of grade downwards, one change of grade upwards. This is a closer approximation to the clinical grading than that given by the quantitative results, in which there were nineteen changes of grade, five down and fourteen up, and is more consistent, since all but one change in the same direction.

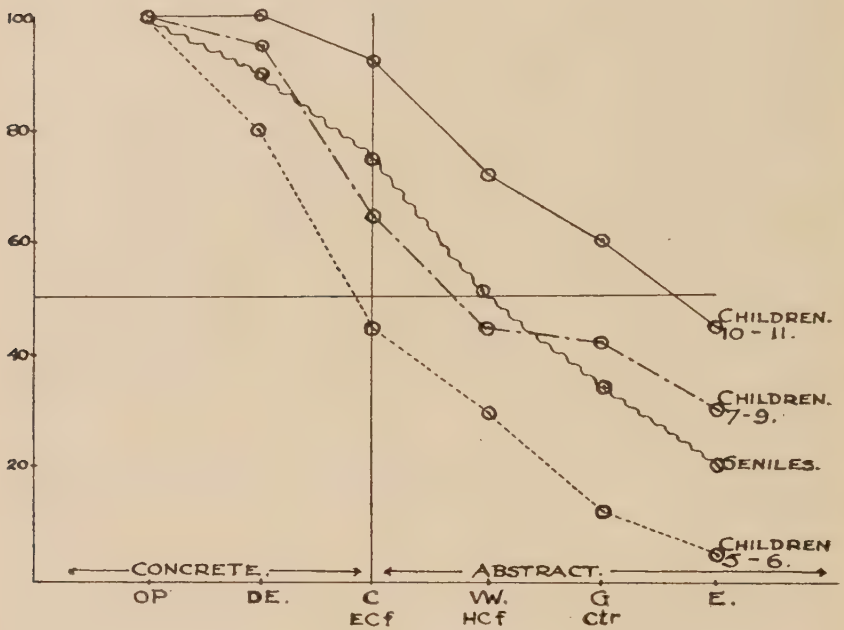
2. The decline in ability to abstract for the group is shown in Graph I. For comparison the results on the same test of 123 children aged 5–11 were obtained and treated similarly. The youngest children aged 5–6 show less than 50 per cent. of ability to abstract in the easiest abstract problems, and that ability falls to zero as the problems increase in difficulty. Ages 7–9 and seniles are practically equivalent in growth and decline respectively of the ability to abstract, and it is interesting to note that the children show some signs of the plateau common in learning curves while the seniles show a smooth falling off in ability. The ability to abstract appears clearly in the 10–11 age-group, and falls below 50 per cent. only when the most difficult problems are reached.

Graph II shows similar results with the least demented seniles approaching the 10–11 age level and the most demented seniles little better than the 5–6-year-olds.

The problems were ranged according to the percentage in each group passing each problem and the scatter analysed.

The extent of the scatter and its position in the scale is an indication of the extent to which that particular type of problem is within the powers of the group. For the easiest type of problem the scatter is a maximum for the 5–6-year-olds and a minimum (zero) for the 10–11-year-olds. For comparison (Graph IV) the

GRAPH No.1.




GRAPH I.—Percentage of each age-group passing each type of problem.

————, age 10–11. ~~~~~~~, seniles.
— · — · —, age 7–9. - - - - - - - - age 5–6.

O.P. = overall pattern. H.Cf. = harder configuration.
D.E. = discrete elements. G. = gestalt.
C. = continuity. Ctr. = contrast.
E.Cf. = easy configuration. E. = eduction.
V.W. = varying width.

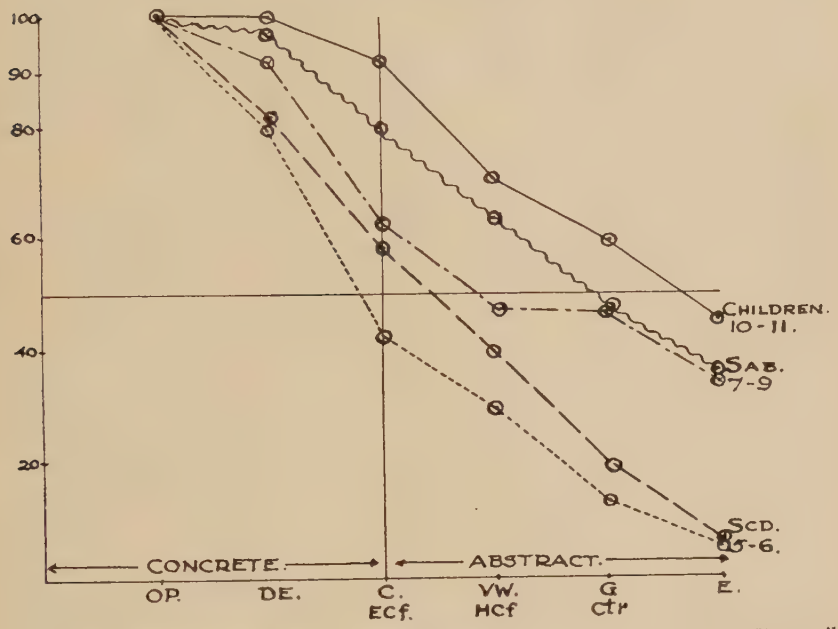
scatter for the SCD group has been superimposed on that for the 5–6-year-olds (dotted lines represent SCD scatter). The scatter for SAB group is superimposed on that for the 10–11-year-olds (broken lines represent SAB scatter). This shows that the SCD group have the same grasp of the easiest problems as the 5–6-year-olds, but have a much better grasp of all configurational problems. In eduction problems the groups are about equal. SCD compares favourably with the 7–9 group in configuration and education problems. The SAB group is superior to the 5–6 and 7–9 groups, and compares favourably with the 10–11 group except in eduction problems. This confirms the qualitative differences between children and seniles already noted, and is perhaps a reflection of the difference between grasping and losing the ability to abstract which was suggested in Graphs I and II.

3. The score beyond the intellectual level reached depends on whether the patient continues to attempt problems using the correct principles of earlier and easier problems within his grasp. If he does so continue, he builds up his score ; if he does not, but chooses a high proportion of random responses, his score increases little beyond that of his level.

The patients were assessed clinically in terms of emotional stability. It was then found that the emotionally stable patient, in solving say eduction problems beyond his scope, would apply the principles successfully used in the simple configuration problems, and so, although not correct, would add to his score. Other patients when solving problems beyond their capacity, break down, showing agitation, instability or evasion and choose many totally irrelevant answers. Previously won experience appears not to benefit such patients.

The loss of ability to abstract, therefore, appears to determine the level of difficulty which the patient can master, but his total efficiency is a function not only of this loss, but also of his emotional reaction to the loss.

GRAPH No. 2.




GRAPH II.—Percentage of each age-group passing each type of problem. The senile group is split into two sections, SAB—less demented, SCD—more demented.

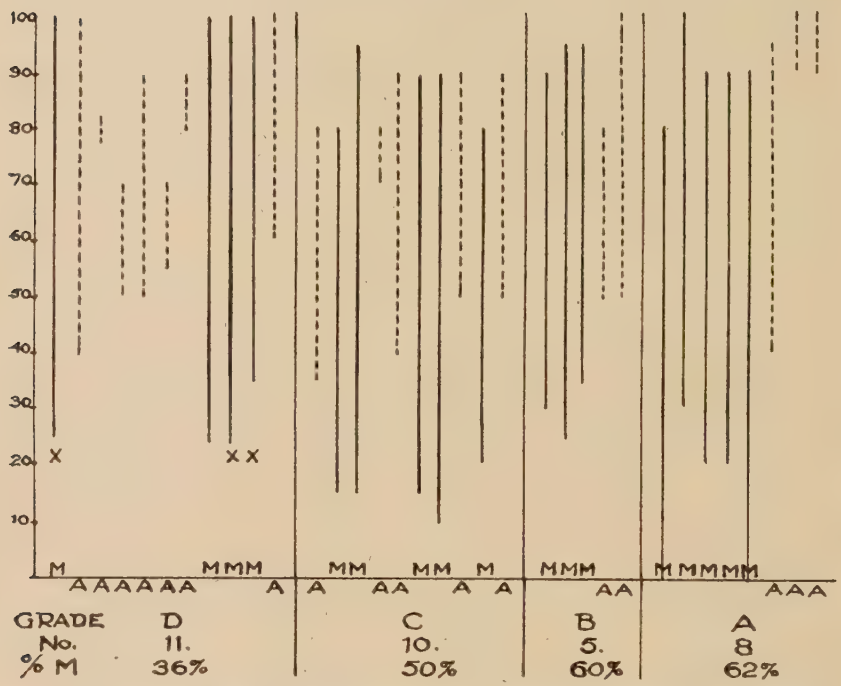
———————, age 10–11. — — — — — —, SCD.
~~~~~~~~~~, SAB. - - - - - - - - - - -, age 5–6.
— · — · — · —, age 7–9.

By determining the ratio between the percentage marks up to the limit of problem difficulty reached, and the percentage score in problems beyond that point, a rough index of emotional adjustment to deterioration is given. Graph III shows these percentages for each patient. It is interesting to note that the number of poorly adjusted patients increases in each group up to a maximum in the least demented group. Presumably as the degree of dementia increases the realization of its effect is less, so that the least demented group is more acutely aware of the deterioration. This was borne out by the demeanour and comments of the patients during the test. Irritability, questions as to the point of the test, attempts to mask failure, etc., varied inversely with dementia.

All grades of seniles showed the same general characteristics of approach to the tests, the worst and best groups being differentiated by degree only. There was a slowness to comprehend the instructions, which had to be repeated several times before the start and several times during the test. Group E would proceed with the test after each instruction, and would often fit a piece in two or three times in as many minutes without any memory of having tried it before. Groups C
~~~~~~~~~~

and D were characterized by asking for guidance, and a few patients would hardly touch a piece before some reassurance. These groups also made many excuses, and responded eagerly to flattery and encouragement. In the top grades, A and B, considerably more annoyance was shown. Sometimes the same piece would be fitted in a number of times with the realization that it was wrong, and increasing

GRAPH No. 3.




GRAPH III.—Marks gained by each patient after he passed his limit of fully correct solving compared with his total up to that point ; a fall of greater than 60 per cent. was taken to indicate poor adjustment to his deterioration. Grades A to D represent progressive stages of dementia.

——————— M, poorly adjusted.
- - - - - - - - - A, adjusted.
x cases in which clinical estimate differs from psychometric estimate.

irritation because the error could not be seen. This type of behaviour usually ended with an outburst of temper, or the examiner was dismissed with the advice to have a younger person do the test.

*Comparison with Children.*

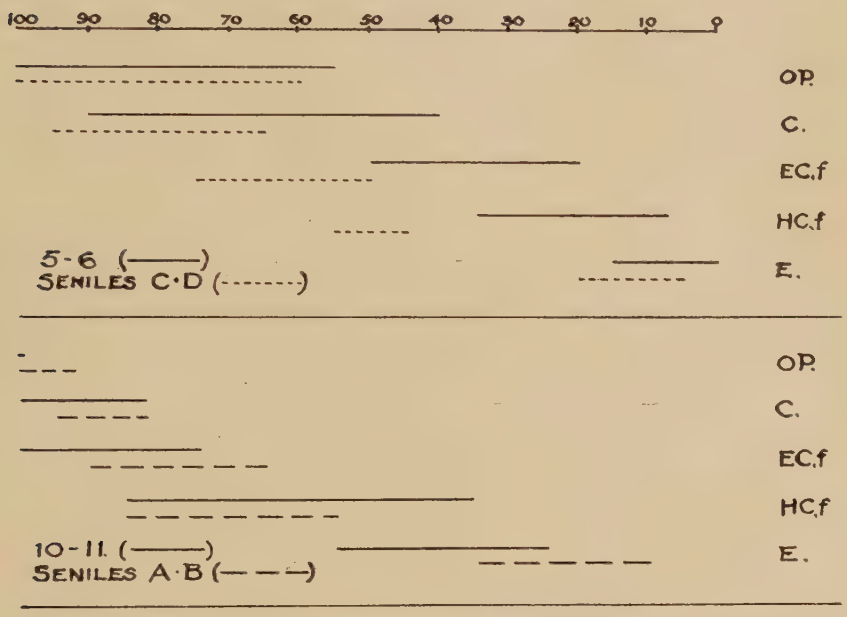
The question arises whether the senile group shows simple regression to the childhood level, or whether any difference is apparent in the quality of performance or method. Quantitatively the seniles may be equated with different childhood stages with an average around the eight-year-old level. Eysenck (7) gives this as her senile average attainment in Matrices. We were more interested in the patients' method of attack on a problem than in comparing end-results.

*In the continuity type of problem* seniles and children tend to solve on the overall pattern level. Common errors in this type of problem are : Age 5–7, confusion of figure ground (e.g., in Set A 6). Where an incomplete answer is given the younger child seems to leave out the horizontal part while the older child leaves out the vertical part. In the seniles the same tendency to solve by overall pattern is shown,

but the E group equivalent in level to the younger children shows not the omission of horizontal, but the vertical incomplete pattern of the older children.

*In varying width problems* the youngest children are content with a response which shows varying width without bothering about continuity, sometimes even without considering the direction of the lines. The older children and the less deteriorated seniles get both varying width and continuity elements even when they fail to get the correct solution. The senile groups C and D are similar to the youngest children in that they get only one element—varying width or continuity, but not both—but are different in that they go sometimes for the one and sometimes for the other.

GRAPH No. 4.




GRAPH IV.—Compares the scatter of performance and its position in the scale for seniles and children. The scatter of the more demented seniles (dotted lines) is compared with that of the 5-6-year-old children (straight lines), that of the less demented seniles (broken lines) with that of the 10–11-year-old group (straight lines).

O.P. = overall pattern. H.Cf. = harder configuration.
C. = continuity. E. = eduction.
E.Cf. = easy configuration.

*The configurational problems* show greater differences between seniles and children. Group E solve almost entirely by whole responses. The youngest children vary their responses, sometimes answering in wholes, but equally frequently they respond with repetition of one of the elements, horizontally, vertically or diagonally. The difference appears to be that the seniles see the pattern as a whole, i.e., they can integrate the elements, but fail to see that only one part is needed to complete the pattern. The youngest children cannot integrate but see only discrete elements. Groups C and D range their responses from wholes to repetitions, but their repetitions are chosen vertical or horizontal to suit the configurational idea. That this is not the case with the youngest children is shown by the indiscriminate diagonal repetition, which rarely fits in with any configuration. The 10–11 age-group and senile groups A and B show less whole responses and more repetitions consonant with configuration.

This suggests that there is a difference between senile groups C, D and E, and the children, while with the older children and the best seniles (A and B) the differences are less marked.

## Discussion and Conclusions.

Returning to the difficulties mentioned in the introduction in the application of tests to a group of seniles, we have mentioned the tendency of some authors, in dealing with the problem of differential decline of various abilities, to use many tests—sometimes up to twenty being used. The time for such a battery has been one hour or more, sometimes a total of two or three hours. It is extremely difficult to hold the attention of seniles for so long, since they lack adequate incentive, and are easily prone to mental fatigability and memory lapses. It seems obvious that these extensive batteries defeat their own purpose by their very extensiveness.

Further, the formal application of tests with instructions standard for young people or normal adults is not valid for the senile group. There must be some latitude in instruction, permission to repeat the instruction often, answer questions and objections, in order to ensure continued general interest, and if these liberties are taken with the tests, the standardization which has been obtained on a totally different group is of limited use.

These difficulties make formal quantitative scoring inadequate. They open the way for a specialized approach in testing which takes into account the difficulties peculiar to this group and allows a modification of test instructions, timing, spreading of items, etc., to suit the individual. The Board Form of Progressive Matrices is adaptable to this purpose.

Special techniques of testing and marking are required, and the contribution of the technique described here is to combine the assessment of deterioration with an assessment of the emotional reaction to it. Deterioration in senility involves decline in the cognitive, affective and conative aspects of mental ability (as well as decline in physical powers). Previously the emphasis was placed on the cognitive decline, although lip service has been paid to these other aspects. Here it is shown that the emotional reaction affects the total performance and may change the intellectual level reached ; e.g., in five cases of catastrophic reaction to the test situation there was something like a total collapse at the start of the test and the easy introductory items were badly done.

Superficially, intellectual level of various grades of dementia can be equated with intellectual level of various age-groups of children. Closer investigation of the popular errors in different types of problem shows differences in approach by seniles and children, the main differences being :

(1) Younger children often confuse the figure-ground of the problem. E group of senile, although equated to this children's group in level show this confusion less often.

(2) There is a wider variation of error in the children, although in E group of seniles there are more random responses. The E group also follow the older children in leaving out vertical lines rather than horizontal.

(3) All senile groups except E make some attempt at dealing with the complexities. Young children and E group can deal only with one complexity at a time.

(4) Young children almost invariably fail to get the idea of configuration, and vary their responses by repetition of elements. Seniles E see the pattern as a whole, and the repetition response of other grades of seniles is always chosen with regard to the configuration.

The possibility of measuring deterioration quotients has been discussed, and the commonly accepted index of deterioration shown to be of doubtful validity in view of the falling off in vocabulary level.

Seniles lose abstract ability gradually, and present in the group a picture similar to the growth of this ability in children. The most demented have lost their ability, and are equivalent to children aged 5–6 who have not yet gained it. The medium group are in process of losing it, and compare with the 7–8–9 group who are in process of gaining it. The best group retain something of the ability, and compare with the 10–11 group who are in process of consolidating a newly acquired ability.

In spite of this broad equation of sub-group of seniles with sub-group of children, there are differences in the approach to the problem and the methods of solving in each group which distinguish the performance of seniles from that of children, though the test score or mental age may be the same.

## Summary.

The importance of the aged community has been realized recently, and has caused a re-examination of the methods of assessing mental deterioration. A review of the literature shows that, while the purely quantitative approach is now known to be inadequate, little attempt has been made to deal with the problem qualitatively, apart from descriptive treatment of results.

This paper presents a method which combines quantitative and qualitative data, and attempts to relate emotional reaction of the patient to his deterioration. The method has been applied to a series of forty senile-arterio-sclerotic patients treated in a mental hospital.

It is shown that, while the loss of ability to abstract determines the level of problem difficulty which the patient can master, his total efficiency depends not only upon this loss but also upon the emotional reaction to it.

The results of the senile group were compared with those of children.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# CONCEPTUAL IMPAIRMENT IN DEPRESSIVE AND ORGANIC PATIENTS OF THE PRE-SENILE AGE GROUP.

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The problem of differentiating, in patients of the pre-senile age group, the degree and quality of intellectual impairment that is due to depression from that which is brought about by some organic, cerebral deterioration is one of some practical importance. It is, in fact, as Henderson and Gillespie (1950) stress, an important point to determine with regard to the prognosis of depressive cases of this age " whether or not there is any complicating organic process causing a failure of memory and efficiency. If such is present then the prognosis must be viewed much more gravely than would otherwise be indicated."

There seems, however, to be considerable difficulty in achieving this differentiation on the basis of test findings, and, clinically, the problem appears very complex, as judged, for instance, by White's (1935) inclusion of the involutional psychoses in the pre-senile group.

With regard to the pre-senile psychoses, Alzheimer's and Pick's disease, Goldstein and Katz (1937), from a careful study of a case of Pick's disease, maintain that, on the basis of psychological changes, it is possible to distinguish such a case in its early stages from involutional melancholia. Apart from the later and more specific psychological symptoms, the authors suggest that one outstanding feature is the extreme " concreteness " of the patient's attitude, as inferred from her performance on a simple task of copying with matches designs exposed tachistoscopically. The only designs which this patient was said to be able to recall and reproduce accurately were those which she was able to name, as where an inverted " V " was called a roof. However, such a naming reaction, with perceptual material of this kind, is so common even in normal people that the value of this sort of uncontrolled observation is very dubious. Certainly there seems little use in describing such a reaction as pathologically concrete, and, as Hebb (1945) points out, one would be more inclined to describe naming an inverted " V " a roof as involving some process of abstraction. This patient was of low intelligence, so that the observations can be of little general value in aiding the discrimination of pre-senile dementia from involutional melancholia. Stengel (1943), in a study of the symptomatology and differential diagnosis of Alzheimer's and Pick's disease, suggests, in fact, that " further research may reveal that there exists a more than superficial relationship between Alzheimer's disease and the deteriorating type of involutional melancholia."

We find, then, that the problem of clinical differentiation of organic from depressive, particularly involutional, syndromes within this age-group is often a matter of some difficulty and uncertainty. This suggested close relationship between some of the syndromes makes the likelihood of differentiating them at all clearly by test results rather problematic.

There appear to be few psychometric studies of impairment in patients of this age-group. Jones and Kaplan (1945), in reviewing the literature, point out that " the pre-senile psychoses have been almost untouched by formal psychological inquiry, and involutional melancholia has not been extensively investigated by psychological methods." The writers believe that standard tests, designed specifically for younger people, are not wholly valid with patients of this age, and suggest, with regard to the involutional melancholic, that " since there are no demonstrable brain lesions, with adequate co-operation, one would expect no important changes (as compared with normals) except the general slowing down of reactions, characteristic of this psychosis."

Psychometric investigations, such as those of Rapaport (1945), using the Wechsler scale, and the findings of Wechsler himself (1944) on intellectual deterioration, have produced various test patterns, signs and ratios of some indirect but uncertain relevance to our present problem, but little, if any, adequate investigation

has been made of the more specific differentiation of depressive impairment from organic deterioration. It seems doubtful, in fact, whether the available quantitative measures of deterioration are at all helpful in this respect. We can therefore summarize what seems to be the present position, regarding both the clinical problem of differentiation and the mental test contribution to this problem, as follows :

1. Clinically, the weighting of depressive and organic features in the symptomatology of some patients of this age-group may be very hard to discern, as there is much apparent continuity and overlap from one syndrome to another.

2. Mental test results, using standard intelligence scales or batteries, may provide quantitative estimates of deterioration, but interpretation of the nature of the deterioration still must depend upon clinical skill and impression in picking on distinctive qualities of failure. Qualitative results, such as those of Goldstein and Katz, lack precision and adequate control.

The main object of the present investigation has therefore been to try and discover, first, how useful one of the standard tests is in differentiating the depressive from the organic aspects of impairment, and secondly, to devise a short set of conceptual tests which might, according to Goldstein's general hypothesis, more clearly bring out the organic features where these are present.

## Method and Test Materials.

For this study the age range of the patients was fixed as from 41 to 65 inclusive. So as to try and differentiate those aspects of impairment due to depression from those primarily due to organic brain change, patients were rated psychiatrically as falling into one of three groups :

Group I : Cases showing a clear depressive symptomatology, with no evidence of a complicating organic process.

Group II : Cases showing clear evidence clinically, from physical examination, C.S.F., air encephalography, or E.E.G., of some primarily organic syndrome, such as early senile dementia, cerebral arteriosclerosis, or pre-senile dementia.

Group III : Cases where the presence or absence of organic features is clinically uncertain.

The total number of patients studied was 70. The distribution according to clinical group and sex is as follows :

| Group. | Male. | Female. | Total. |
|---|---|---|---|
| I | 6 | 20 | 26 |
| II | 18 | 10 | 28 |
| III | 7 | 9 | 16 |
| Total | 31 | 39 | 70 |

The patients were referred psychiatrically on admission in the usual way, with a request for report on intelligence level and any deterioration present.

The tests used were as follows :

### I. *Wechsler Adult Intelligence Scale.*

#### 1. *Vocabulary Level.*

The Vocabulary test of the Wechsler adult intelligence scale was used to give some criterion of prepsychotic attainment level.

#### 2. *Wechsler " Hold " and " Don't Hold " Tests.*

Six of the Wechsler subtests (3 verbal, 3 performance) were given in order to obtain a present I.Q. level and a measure of intellectual deterioration. Scores on 3 of the subtests (Vocabulary, Picture Completion and Object Assembly) are classed as holding up with age, the remaining 3 (Digit Span, Block Designs and Digit Symbol) being " don't hold " tests. Deterioration ratios are calculated in the usual way (Wechsler *op. cit.*, chapter vi), the normal age correction being made. Some patients, however, showed no *positive* deterioration (i.e., no percentage loss beyond that to be expected at the patient's age), and it was decided to calculate, in these cases, how much *negative* deterioration they showed (i.e., how much, relative to age, they were *better* on the " don't hold " tests than on the " hold ").

## II. *Conceptual Tests.*

1. *Quality of Vocabulary Definition.*

The usual vocabulary score that is used for assessing prepsychotic attainment level takes little account of the level of definition that the subject employs. Scoring criteria are not rigorous, and the score obtained may be said to represent more the number of correct recognitions that the subject makes than the use to which he is able to put the words. Yacorzynski (1941) asserts that vocabulary scores may be maintained in later maturity chiefly because there are many different, acceptable ways of defining words. He points out that deterioration may have eliminated some of the more difficult definitions or more elaborate contextual meanings, without disturbing the obtained scores.

The first of the conceptual tests was therefore devised in order to find out the patient's preferred level of definition for 10 common words. Each word was printed on a separate card, and opposite it were printed 6 short sentence-definitions of the word's meaning, each having some degree of relevance to it, but varying approximately from a conventionally acceptable general definition down to one that was inessential and irrelevant. Order of arrangement of the sentences was varied from card to card.

The 10 words used were : ship, cupboard, dog, newspaper, water, flower, apple, pencil, coal, hat.

The 6 sentences for the word " apple " will give an idea of the task involved. These are :

*Apple.*

You make cider from it.
You eat it.
It's round and hard.
It has a skin or peel.
It's a fruit.
It's good for you.

The patient was told to read all the sentences on the card, and then to choose the one which he thought gave the best general meaning for the word. Further explanation was given, if the patient was hesitant and doubtful about the task. No example of a " correct " answer was given, because it seemed that the spontaneous choice of the patient would be the more revealing of his general attitude and level of comprehension.

*Scoring :* + 1 was given for each " correct " choice (total + 10). — 1 was given where a patient chose one of the " least relevant " definitions, or where he " spoiled " his response by indeterminate reference to several definitions (total — 10)

2. *Sorting Test.*

This test has already been described fully elsewhere by the present writer (Hall, 1951). Briefly, it consists of 12 counters, having 2 different colours, 3 different shapes, 4 different numbers of black squares, and 6 different numbers of blue dots. Sorting can therefore be carried out by progressive stages into 2, 3, 4 or 6 groups, according to the instructions given, there being only one correct method of solution at each stage, except for the 6 grouping, which allows of 2 alternatives. Standard instructions are given carefully and repeatedly if necessary.

*Scoring :* No time limit or time credits are used in the present scoring system, + 1 being given for each correct solution. In addition, *minus* marks are given where any of the following incorrect and negative aspects of performance occur :

(i) " Patterning " the pieces by fitting them closely together.
(ii) More than two repetitions of the original instructions required.
(iii) An irrelevant non-conceptual solution other than (1) above.
(iv) Marked perseveration from one stage to the next.
(v) " Patterning " at stage 2 after being shown correct solution for Stage 1.

By this system some of the qualitative signs of failure, together with the degree of their persistence, are embodied in the final score.

3. *Wechsler Similarities.*

This test was used, with scoring modifications, in order to find out something more about the " giving differences " tendency that was early on observed to be common in some patients of this age group. In the present system the usual

correct responses, according to Wechsler's criteria, are scored + 1 or 2, but any deviant and irrelevant response, such as, for the orange-banana similarity, " Well, an orange is round, a banana is long, so they're different," is scored — 1. The examiner then prompts the patient that a likeness or similarity is required, and, if the patient persists in this kind of answer, a second minus score is given. It is therefore possible to score + 2 for an answer, but, at the same time, to score a minus as well owing to the " spoiling " of the response by irrelevancy or difference.

4. *Picture Conception.*

The test material consists of pictures of 3, 4 or 5 everyday objects taken from the Binet material, and pasted in groups on cards in such a way that all the objects in a group have some common function or belong to the same general catagory. The task then is to describe what each group has in common. For demonstration, the patient is shown a card with pictures of a pen-knife,a pair of scissors, and a table knife on it. It is then clearly explained that the examiner does not require the patient to name or specify each individual object, but only to say that, in this instance, they are all means of cutting. The remaining 4 cards of the test are shown with repetition of the instructions.

*Scoring :* Scoring is much the same as for Similarities and Sorting. + 2 is given for each " correct " answer, or + 1 if a correct answer is only given after prompting or where the answer is not adequate for the + 2 criteria (total + 8).

— 1 is given if individual naming of the objects takes place or if a " difference " remark is made. A second — 1 is given if such a tendency persists after further prompting (total — 8).

In general, therefore, the + and — system used for these 4 tests has been devised to try and take into account the " deviant verbalizations," and the irrelevancies in the conceptual approach of some of the patients. In this way, it was hoped that the score might represent more accurately the *degree of persistence* of the conceptual failure, which, it was supposed, might distinguish the organic from the depressive.

## Results.

1. *Clinical Material.*

The clinical categories into which the 70 patients tested in this study fall are shown in Table I below, together with the frequency with which they occur in the male patients (M) and female (F).

Table I.

| Organic group. | | | |
|---|---|---|---|
| Clinical category. | M. | F. | Total. |
| Presenile dementia | 1 | 2 | 3 |
| Huntington's chorea | 1 | — | 1 |
| Treated G.P.I. | 2 | — | 2 |
| Organic epilepsy | 3 | — | 3 |
| Disseminated sclerosis | 1 | — | 1 |
| Cerebral arteriosclerosis | 5 | 2 | 7 |
| Post-encephalitic Parkinsonism. | 1 | — | 1 |
| Toxic states | 3 | 1 | 4 |
| Depressive or paranoid states with early dementia | 1 | 5 | 6 |
| Total | 18 | 10 | 28 |

| Depressive group. | | | |
|---|---|---|---|
| Clinical category. | M. | F. | Total. |
| Involutional depression | 2 | 8 | 10 |
| Recurrent depression | 2 | 8 | 10 |
| Mixed depressive states | 2 | 4 | 6 |
| Total | 6 | 20 | 26 |
| **Doubtful group.** | | | |
| ? Presenile dementia depression | 1 | 1 | 2 |
| Remainder all show some variety of depressive syndrome together with possibility of early dementia of organic change due to vascular disorder | 6 | 8 | 14 |
| Total | 7 | 9 | 16 |

2. *Age, I.Q. and Vocabulary Scores for the 3 Groups.*

Average, Range and Standard Deviation for age, I.Q. and Wechsler Vocabulary raw scores for the three groups are given in Table II.

TABLE II.

| | | Organics. | Doubtful. | Depressives. |
|---|---|---|---|---|
| Age | Average | 55·8 | 57·6 | 54·0 |
| | Range | 42–65 | 41–65 | 40–64 |
| | S.D. | 6·867 | 5·613 | 6·585 |
| I.Q. | Average | 99 | 104 | 105 |
| | Range | 76–130 | 77–118 | 80–128 |
| | S.D. | 14·865 | 11·060 | 12·265 |
| Vocabulary raw score | Average | 22·5 | 22·1 | 25·2 |
| | Range | 9–35 | 16–25·5 | 14–37·5 |
| | S.D. | 6·988 | 3·720 | 5·502 |

Age distributions for the three groups are similar, although there is rather less scatter in the doubtful group, in which there is only one patient below age 50. Wechsler I.Q. distributions show a considerable range, with the organic group average somewhat lower and the S.D. greater than in the other two groups. The Wechsler Vocabulary raw scores show the depressives to have a rather higher average, while the lower range in the organic group includes three patients who score only 9 on vocabulary.

3. *Wechsler Deterioration Ratios and Verbal-performance Scores.*

In Fig. 1 are shown the distributions of deterioration ratios, both positive and negative, for the three groups of patients. Total N is 65, as 5 of the 70 cases were not given the full set of Wechsler tests.

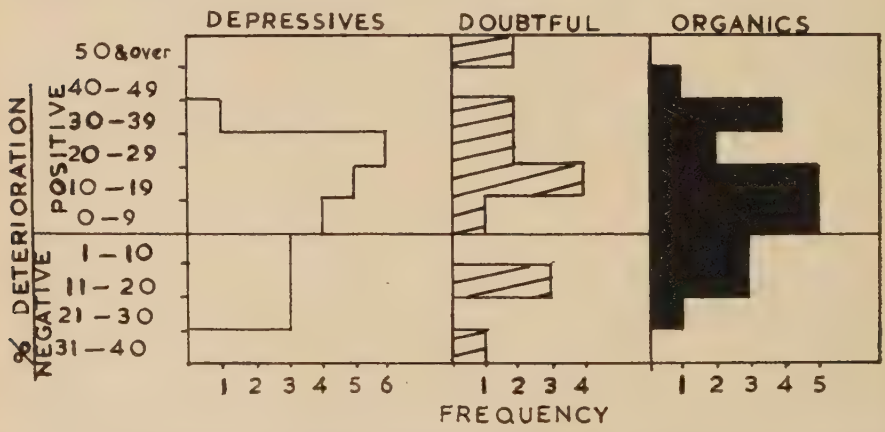


FIG. 1.—Distributions of positive and negative deterioration percentages for 65 patients on the Wechsler scale.

The histograms show that the distribution of deterioration percentages is very little different in the depressive and organic groups. The difference between the means (depressives + 5·3, organics + 7·7) is not significant. The conclusion would seem to be that the deterioration percentage is of little, if any, use in helping to discriminate organic deterioration from depressive impairment. This confirms previous work by Botwinick and Birren (1951) on senile psychoses, in which it was found that the ratio did not differentiate reliably a senile group from a normal group of comparable age. The high proportion of negative percentages is perhaps surprising (9 out of 25 in the depressive group, 7 out of 25 in the organic, and 5 out of 15 in the doubtful group). This is sometimes due to the fact that tests like Picture Completion and Object Assembly do not hold up, or, as occurred in two of the toxic organic cases, Memory for Digits has the highest score.

Secondly, Wechsler's contention that discrepancy between verbal and performance I.Q. may have some diagnostic significance in that " organic brain cases, with few exceptions, do consistently better on verbal than on performance tests " (*op. cit.*, p. 153) is not supported by our present findings. Although, in the writer's experience, this relationship may hold good in some organic syndromes, for example G.P.I., it is certainly not generally true of organic psychoses of this age-group, as is clear from the histograms of Fig. 2. Neither does our present data seem to give any general support to Rapaport's (1945) finding that performance scores tend to be reduced more than verbal in depressive syndromes. While again this relationship may hold good in some cases, it is scarcely a reliable diagnostic aid.

The histograms of Fig. 2 show that there is no general tendency for patients of these 3 groups to have higher verbal than performance I.Q's., only 13 out of

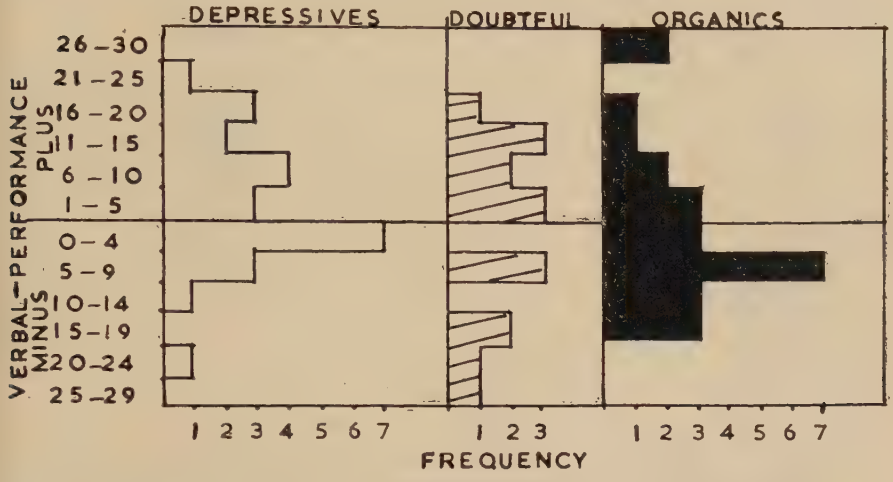


Fig. 2.—Distributions of verbal-performance discrepancies for 66 patients.

25 depressives, 9 out of 16 doubtful, and 12 out of 25 organics showing this pattern. In the organic group there is actually an opposite tendency for the patients to have higher performance than verbal I.Q's. (the mean verbal-performance discrepancy for this group is — 0·72, as compared with + 3·16 for the depressives).

There is one further point about these distributions that should be noted. It is the possibility that there may be some sex difference contributing to the difference between the verbal-performance distributions for depressives and organics, as the proportion of M : F is 18 : 10 in the latter group and 6 : 20 in the former. Although Wechsler does not seem to have found any such difference in his normal population, it does not seem possible to discount this factor.

With regard, then, to the value of the Wechsler scale in differentiating depressive from organic features in patients of this age-group, we must conclude that neither the deterioration ratio nor the verbal-performance relationship is of any reliable discriminative value. In case material of this kind, where very few even of the organic patients are described clinically as more than moderately deteriorated, even the more incidental qualitative signs, such as poor digits backwards in relation to forward span, and conspicuous " symbolic " failure on block designs, are comparatively rare.

4. *Conceptual Test Results.*

On the basis of the plus and minus scoring system already described, there is a far clearer differentiation between organic and depressive than any apparent patterns on the Wechsler scale can produce. The histograms of Fig. 3 show the distributions of the plus and minus score discrepancies for each of the three groups.

The difference between the means for the depressive and organic groups (+ 16·73 and + 0·75 respectively) is highly significant ($t = 4·459$, giving a probability of

chance occurrence of considerably less than ·01) although there is, as one would expect with such clinical material, quite a lot of overlap. The organics tend to have a greater proportion of minus signs than the depressives. Although the latter may show minus tendencies, such as giving differences on Similarities, and even the " patterning " behaviour on the Sorting test, they tend not to *persist* in these tendencies when prompted and when the nature of the conceptual task is

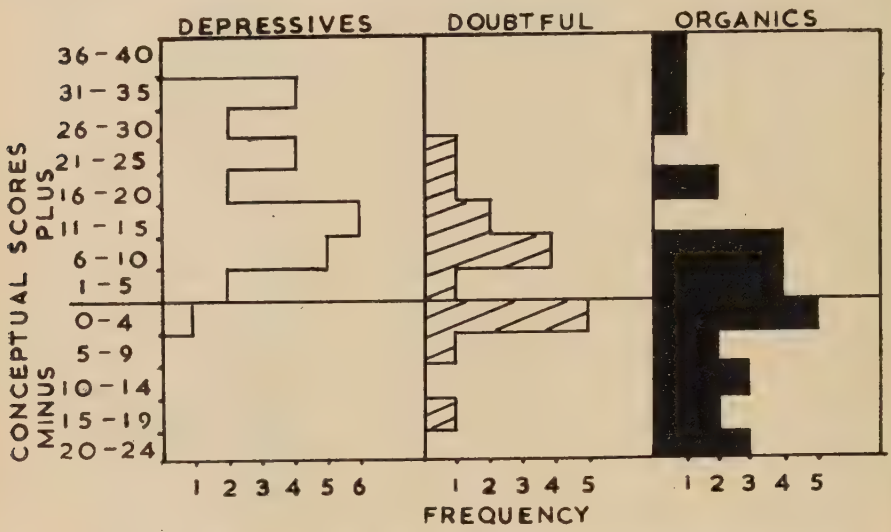


FIG. 3.—Distributions of conceptual plus-minus discrepancies for 70 patients.

again explained. There is, one might say, especially with reference to the involutional type of depression, little to differentiate some of the " borderline " depressives from the organics except the greater degree of adherence to non-conceptual responses. The " doubtful " cases tend to fall more within the organic distribution than the depressive.

The average plus and minus scores on the 4 conceptual tests are given in Table III.

TABLE III.

| | | Organics. | Doubtful. | Depressives. |
|---|---|---|---|---|
| 1. Qualitative Vocabulary . | + | 5·0 | 5·6 | 6·3 |
| | − | 4·5 | 4·1 | 3·2 |
| 2. Sorting test . . . | + | 0·9 | 0·9 | 2·6 |
| | − | 3·0 | 2·9 | 1·0 |
| 3. Similarities . . . | + | 7·2 | 7·8 | 12·5 |
| | − | 5·0 | 4·6 | 2·4 |
| 4. Picture Conception . | + | 3·5 | 4·6 | 6·2 |
| | − | 3·4 | 2·9 | 0·7 |
| Total . . . | + | 16·6 | 18·9 | 27·6 |
| | − | 15·9 | 14·5 | 7·3 |

As the histograms of Fig. 3 have shown, there is little to differentiate the doubtful cases from the organics, while there is a consistent and marked difference between organics and depressives.

Within the depressive group there is some evidence that those patients classified as involutional depression come nearer to the organic group in plus-minus conceptual scores than do the other kinds of depression. Whereas only 1 out of 10 involutional depressives has a conceptual discrepancy score of above plus 15, 11 out of the 16 other depressive patients score above plus 15. There is a highly significant difference between the mean scores for these two sub-types of the depressive group ($t = 3{\cdot}732$, with probability of chance occurrence less than ·01).

The average vocabulary scores for the two subgroups are very similar (Involutionals 24·8, other depressives 25·4), while the non-involutional group has an average age 5 years greater than that of the involutional. This observation is in keeping with the clinical rating which tends to place the involutionals alongside the cerebral arteriosclerotics on the deterioration scale. This is further confirmed by analysis of the organic group, which shows that all the 7 arteriosclerotic cases overlap with the depressives, 6 of them falling within the middle of the total distribution of discrepancy scores. These differences within the depressive and organic groups are shown in Fig. 4, in which the distribution of conceptual discrepancy scores for each of the 4 subgroups is given.

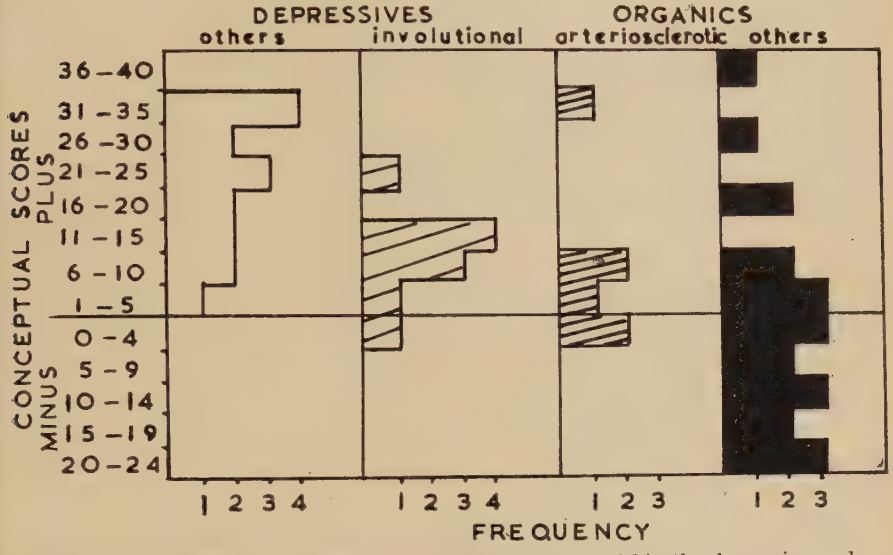


Fig. 4.—Distributions of plus-minus conceptual scores within the depressive and organic groups.

## Summary and Conclusions.

The problem was set of trying to discern, by means of mental tests, whether impairment was due primarily to some early organic brain change or to the degree of affective disturbance in patients of the pre-senile age-group. Seventy patients, male and female, within the age range 41–65, who were clinically rated as falling into one of three groups (definitely organic, definitely depressive, and doubtful), were studied with subtests of the Wechsler adult intelligence scale and also with 4 short conceptual tests. Results showed that gross indicators of deterioration on the Wechsler, such as "hold"—"don't hold" ratios and verbal-performance discrepancies, were unreliable in differentiating the organic from the depressive patient. On the other hand, the conceptual tests, scored with a plus and minus system, differentiated quite clearly between patients of the two groups, although there were exceptional cases who did not conform to the group pattern. Involutional depressives and cerebral arteriosclerotics did not differ markedly from one another on the conceptual scores, tending to come towards the middle of the distribution.

In conclusion, the set of conceptual tests used is short and easy to administer. The scoring of the *persistence* of such tendencies as giving irrelevancies, differences, and so on, although the system and the criteria are not perhaps as yet sufficiently refined, seems to differentiate the organic from the depressive performance with reasonable accuracy. In diagnostic psychological testing, selection of tests which will give the essential information within a reasonably short time is often a consideration of some practical importance for the tester. It would seem that short conceptual tests of this kind together, perhaps, with a short learning and memory assessment, would provide the essential diagnostic data for this particular problem, both reliably and economically.

I would like to thank Dr. R. E. Hemphill for permission to make use of the clinical material for this research. I would also like to thank members of the medical staff at Barrow Hospital for their co-operation, in particular Dr. R. Maggs for providing most of the case material and for his great help in discussing the clinical features of the various cases. Finally, I would like to thank Mr. O. L. Zangwill and Dr. J. McFie, of the National Hospital, Queen Square, for reading the manuscript and for their helpful comments.

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# METABOLIC RESPONSE TO ELECTRICAL STIMULATION IN SEPARATED PORTIONS OF HUMAN CEREBRAL TISSUES.

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Electrical stimulation of different areas of the human brain has hitherto been confined to experiments with the brain *in situ*, in living subjects. It has been carried out while the brain received its blood supply from normal sources. By chemical analysis of the arterial and venous blood and measurement of its rate of flow, information has been obtained on how metabolic changes in the brain vary with changes in its activity. However, these conditions can give information only about gross biochemical changes associated with stimulation; they are cumbersome, and would not indicate abnormal reactions in small areas. Also, they detect differences only in substances which are actively exchanged with the blood stream.

With experimental animals, indirect indications of more localized metabolic events have been obtained by temperature (Serota and Gerard, 1938) and potential (McCulloch, Klein and Goodwin, 1945) measurements. Also, it has proved possible to obtain electrical responses to stimulation in portions of cerebral cortex attached to the animal by blood vessels only (Burns, 1950, 1951; Chang, 1951). It is possible that techniques depending on arterio-venous difference might be applied to such preparations; the isolated portions, however, remain relatively large, and only superficial areas can be at all readily examined.

Radically different techniques have been developed recently in these laboratories whereby metabolic responses to electrical impulses can be measured in fragments of mammalian brain weighing only a few milligrammes, some time after their complete separation from an animal (McIlwain, 1951*a*, *b*). Changes in a variety of metabolites both in the tissue and in surrounding fluids can be followed (McIlwain, Anguiano and Cheshire, 1951; McIlwain and Gore, 1951). The methods would seem to be especially suitable for investigating the properties of portions of the human central nervous system removed at biopsy or during neurosurgical operations. The information which one might expect to obtain from such experiments concerns metabolic activities of the unstimulated tissue, and also the type and degree of various of its responses to electrical stimuli.

The present experiments concern portions of tissue which, although removed for therapeutic purposes, were without obvious defects. They have enabled it to be shown that the new methods are applicable to human cerebral cortex. They form part of a larger series in which comparisons are being made by other workers as well as by ourselves of several characteristics of the specimens, so that these can be correlated with the condition of the individuals from whom the tissues were derived.

In experiments of the present type, periods of an hour or more may elapse between the removal of different specimens from the brain during a given operation, and also between their removal and their examination in the laboratories. For this reason, preliminary studies were carried out to find how long and in what manner cerebral tissues could be kept without marked change in the characteristics being measured. These experiments also are described below.

## Experimental.

*Specimens of human cerebral tissues.*—These were available to us through the collaboration of Mr. Murray Falconer, Director of the Guy's-Maudsley Neurosurgical Unit. Advantage was taken of neurosurgical operations for leucotomy and brain tumours to obtain specimens of macroscopically normal brain tissue. These specimens were removed from subjects under general anaesthesia, care being taken that their blood supply was not interrupted until the last possible moment (usually less than 30 seconds) prior to excision. These specimens were then placed in small, dry, glass or polythene containers. These were surrounded by crushed ice in a vacuum can and brought promptly to the laboratory. Here, arrangements for the metabolic experiment had already been made. The time between removal of the tissue, its preparation and restoring to good metabolic conditions in experimental vessels was between 50 and 100 min. During most of this time (noted in the individual experiments) the specimen was at 0°.

*Tissues from experimental animals.*—Young adult guinea-pigs and rats were stunned by a blow on the back of the neck, the brain removed, and portions prepared as described below. Comparable (usually contra-lateral) portions were stored at 0° for 1–30 hr. in containers as described in the preceding paragraph, and then prepared in the same fashion as the earlier specimens.

*Preparation of tissues.*—Any membranes, pial vessels, and clotted blood were removed. Specimens which were sufficiently large were divided into white and grey matter, or in other ways described later. For *slicing*, blocks with a cortical surface at least 6 × 6 mm. and usually up to 6 × 12 mm. were prepared and slices 0·3 to 0·4 mm. thick cut parallel to that surface. In doing this, the tissue was moistened with the saline to be used in the remainder of the experiment and cut with a strip of razor blading, using a recessed glass slide as guide. While slices were being cut, a second worker removed excess saline from them by draining on a glass surface, weighed them with a torsion balance and transferred them to saline in manometric apparatus. Sometimes slices were weighed, drained or dry, at the end of an experiment instead of or as well as at the beginning. With certain apparatus (see below) several slices from much smaller portions of tissue were used, or slices prepared as above were cut with dissecting scissors into fragments weighing a few milligrammes each. These were handled as described by McIlwain (1951*b*).

Small or irregular specimens were prepared by *chopping* (McIlwain, 1951*b*), i.e., passing razor blading rapidly through the tissue so that it was cut into prisms about 0·2 × 0·2 mm. and as long as the thickness of the specimen (some 1–3 mm.). In later work this was done precisely by a mechanical chopper described in detail elsewhere.

*Metabolic experiments.*—These were carried out while the tissue was immersed in nutrient salines and enclosed in apparatus to which stimuli could be applied. Glucose phosphate saline, employed in most experiments, contained 134 mM-NaCl; 5·4 mM-KCl; 1·34 mM-$KH_2PO_4$, $MgSO_4$ and $CaCl_2$; 13 mM glucose; 10·4 mM-$Na_2HPO_4$ brought to pH 7·4 by HCl, and was saturated with oxygen. Of the apparatus, vessels *A* have been described by McIlwain (1951*a*), and in them slices about 6 mm. square were held between grid electrodes as indicated in Fig. 1A. Vessels *E* (McIlwain, 1951*b*) with concentric wire electrodes were used for slice-fragments or chopped tissue. In each case the observations made during the present studies consisted of manometric measurement of respiration throughout the experiment, and determination of glycolysis by chemical estimation of lactic acid at the end of the experiment, using Barker and Summerson's (1941) method.

The consistency of values for respiratory rate is illustrated by the results of the first part of Table I. With the apparatus and procedure chosen, the respiratory rate of a specimen could be determined with an accuracy of about 5 per cent. by 5 or 6 scale readings over a period of 30 min. The greater variation (S.D. 7·5) from the mean value of 70 μmol./gm./hr. shown by the results of Table I is attributable to these results being from different animals in separate experiments over a period of several months.

*Electrical stimulation* was by diphasic condenser pulses from the circuit given in Fig. 1A of McIlwain (1951*a*). The voltage and duration of the pulses were measured with an oscilloscope (Cossor, model 1049) during the experiment.

TABLE I.—*Effect of Keeping at 0°, on Normal and Electrically Stimulated Respiration of Slices of Rat Cerebral Cortex.*

Values during stimulation are in italics and followed by the stimulating voltage in parentheses.

| Time at 0° (hr.). | Respiration (μmol./gm./hr.) in successive 30-min. periods. | | | |
|---|---|---|---|---|
| | 1st. | 2nd. | 3rd. | 4th. |
| 0 | 73 | 73 | 73 | 73 |
| 0 | 76 | 76 | 76 | — |
| 0 | 80 | *102* (15) | *102* (19) | — |
| 0 | 78 | *117* (19) | *84* (12) | — |
| 0 | 57 | *78* (12) | *114* (15) | — |
| 0 | 60 | *120* (20) | *102* (13) | — |
| 0 | 69 | *96* (13) | *144* (20) | — |
| 0 | 72 | *120* (20) | *84* (10) | — |
| 0 | 75 | *96* (17) | *84* (12) | — |
| 0 | 75 | *126* (18) | *92* (27) | — |
| 0 | 84 | *126* (17) | *112* (27) | — |
| 0 | 75 | *138* (21) | *111* (11) | 73 |
| 0 | 66 | *102* (18) | *84* (10) | 63 |
| 0 | 60 | *140* (24) | — | 85 |
| 2 | 63 | 63 | 63 | 63 |
| 2 | 84 | *123* (20) | *90* (12) | 78 |
| 2 | 84 | *138* (20) | — | 80 |
| 2 | 72 | *114* (12) | *66* (8) | 51 |
| 6 | 60 | 60 | 60 | 60 |
| 6 | 68 | *116* (13) | *92* (20) | 66 |
| 6 | 64 | *80* (16) | *64* (21) | 64 |
| 6 | 60 | *75* (12) | *81* (19) | 60 |
| 17 | 56 | *76* (13) | — | 56 |
| 17 | 46 | *72* (20) | — | 66 |
| 20 | 48 | 48 | 48 | 48 |
| 20 | 48 | *66* (18) | — | 51 |

## RESULTS.

### *Choice of Experimental Conditions.*

Conditions for electrical stimulation of separated cerebral tissues have already been investigated using material from lower mammals (McIlwain, 1951*a*, *b*), and the conditions devised in those investigations were used in the present studies. It was necessary in addition, however, to find the extent to which the tissue could be preserved after its removal from an animal, without major change in metabolic response to stimulation. Krebs (1950) found that the respiratory rate of slices of rat cerebral cortex which had been prepared from brain kept in saline at 0° for 24 hr. had fallen only a little below that of slices from fresh tissue. Nothing, however, was known of the persistence of their metabolic response to electrical stimulation.

*Preservation of tissue.*—Cerebral hemispheres or portions of cerebral cortex from rats and guinea-pigs were kept at 0° (*a*) immersed in an ice-saline according to Krebs (1950) and (*b*) in small containers, otherwise empty and dry. In both cases the rates of respiration and aerobic glycolysis were well maintained. However, the texture of the tissue deteriorated during immersion in the saline even during relatively short periods of 1–2 hr. Specimens swelled slightly and became softer. This did not prevent their being sliced, but the slices from specimens kept in saline were more fragile than those from fresh tissue. Our examination of the specimens in tissue-holding electrodes made greater demands on their physical strength than would normal metabolic practice.

Tissues were therefore kept " dry " (conditions *b*) during the present studies. Data with tissue kept in this way are included in Table I. This shows no appreciable difference in respiratory rate after 2 or 6 hr. at 0°, but some fall after 17 or 20 hr. As all the experiments with human tissues were begun within 2 hr. of removal of the specimens, these results indicate the method of storage to be fully satisfactory from the point of view of the properties of the unstimulated tissue.

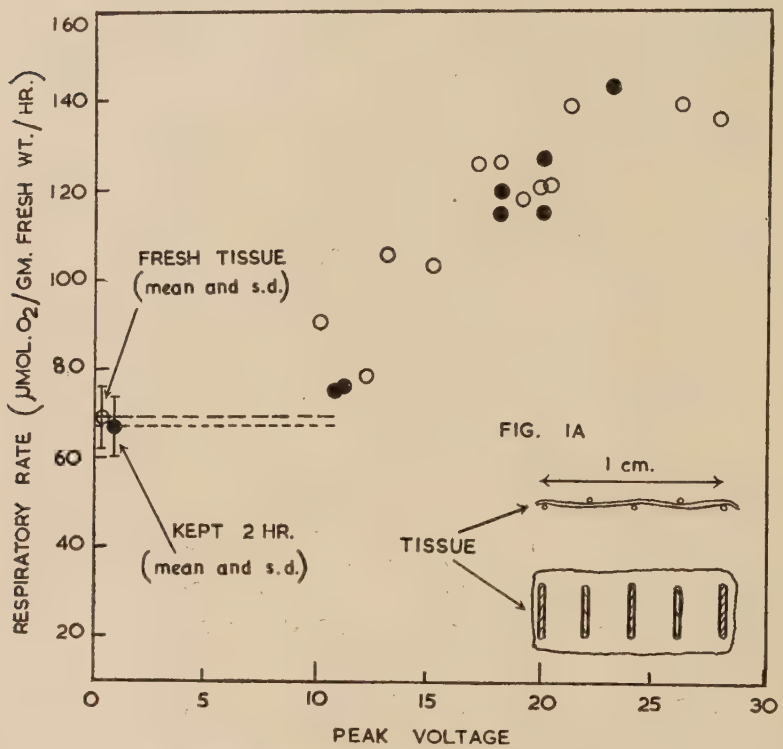


FIG. 1.—Graph. Respiratory response of slices of rat cerebral cortex to impulses of varying voltage. Tissue was in grid electrodes to which were applied condenser pulses of the peak voltage quoted. Pulses were at 100/sec. and of time constant 0·5 msec. Rates refer to the first 30-min. period of stimulation following a period of 30-min. unstimulated respiration, the experimental arrangement being similar to that of Fig. 2.

FIG. 1A.—Grid electrodes. Elevation and plan of tissue in relation to stimulating electrodes. The upper electrodes were connected together to one pole of the output of a circuit similar to that of McIlwain (1951*a*) and the lower electrodes (differently hatched) to the other. The electrode-holder, designed with Mr. H. L. Buddle and Mr. C. C. Kratzing, will be described in detail elsewhere.

*Response to stimulation in fresh and preserved tissue.*—An experiment to establish metabolic response to stimulation was usually planned to comprise four 30-min. periods in which the specimen was successively unstimulated, stimulated at one voltage, stimulated at another voltage, and again unstimulated. With minor modification the periods could have been shortened, but no great advantage was found to accrue from such shortening in the present study. Additional stimulating periods were not included, as the response to the second of the two periods was found to depend to some extent on the nature of the previous period of stimulation. Thus, a submaximal stimulus, following a supramaximal one, gave in some cases a lesser response than when it was applied as the first stimulus.

Fig. 1 shows the effect of a given stimulus, expressed as a voltage-response curve. This indicates that with the fresh tissue a threshold voltage existed below

which a stimulus was ineffective. Response increased with increase in voltage beyond the threshold and up to a maximum response, beyond which further increase in stimulus gave relatively little further response or was deleterious. Impulses throughout the experiments of Fig. 1 were of time-constant about 0·5 msec. and were repeated 100 times/sec. The threshold was then at a peak potential of about 5 v.; the potential at 0·5 msec. after the peak was 1·6 v. With the electrodes used, this latter value corresponded to a potential gradient of 6·5 v./cm. Expressed in this way, the minimal potential gradient giving a maximal or nearly maximal response was 25 v./cm.

Preserved tissues were then compared with fresh with respect to their respiratory response to stimulation. No changes were found except after keeping for periods of 6 hr. or over. Fig. 1 includes values with specimens which were kept "dry" at 0° for 2 hr. before slicing and stimulating. Response by such tissue was not significantly different from that given by fresh tissue. It will be noted that the response to stimulation was determined not only with impulses sufficient to give maximal response, but also with impulses giving suboptimal responses. These might be expected to display better any lack of reactivity resulting from storage of the specimen. No change was, however, detected. The period of 2 hr. extended beyond the time for which neurosurgical specimens were preserved.

After keeping rat brain for 6 hr. at 0°, slices of cerebral cortex prepared from it still responded to electrical stimulation. With peak potentials up to 14 v., the respiratory response was closely similar to that of fresh tissue. However, higher voltages, instead of giving further stimulation, gave less.

### *Metabolism of Human Cerebral Tissues.*

*Unstimulated.*—Respiration of slices of human cerebral cortex has only rarely been measured. The most complete study is that of Elliott and Penfield (1948), who investigated some 24 specimens removed from points which were associated to varying degrees with epileptogenic areas. By comparison of the values between themselves and also with values for the rate of these reactions in normal tissue from other mammalian species, Elliott and Penfield concluded that the rates which they observed were likely to be independent of any pathological change, and that the mean respiratory rates observed were probably those normal to the tissue. With glucose as substrate in a medium containing bicarbonate and Ca salts, values of 0·7–1·6 ml./gm. fresh tissue/hr. (mean, 1·2) were found corresponding to 27–62 μmol./gm. moist tissue/hr. (mean, 46).

In the present studies we have examined some 11 specimens of cerebral cortex, and details of these are given in Table II. Their respiratory rate was determined with glucose as substrate in media containing Ca salts, but buffered with phosphate. The rates were between 22 and 57 μmol./gm./hr. (mean, 40). This appears sufficiently close to Elliott and Penfield's values to support their conclusion that values of this order represent the normal respiratory rate of separated human cerebral cortex. Values for the whole brain *in vivo* are of the same order of magnitude. Considerable variation is, however, to be noted in our values as in those of Elliott and Penfield. In both cases this may be due to local variations in the areas examined, or to the tissue not being from normal subjects. These factors will be assessed later.

In addition, we have examined a few specimens consisting wholly or partly of subcortical white matter, and these indicate respiratory rates for white matter about half as large as those for grey.

Formation of lactic acid during the present experiments has also been examined. The lactic acid produced by slices during aerobic metabolism with glucose as substrate corresponded to a mean rate of formation of 10–20 μmol./gm./hr. Tissue further cut or chopped gave rates up to 30 μmol./gm./hr. These values are similar to those of aerobic glycolysis in other species, but in both cases may be initially higher and fall during the course of the experiments (cf. McIlwain and Grinyer, 1950).

*Stimulated.*—The effect of electrical stimulation on the respiration of human cerebral cortex and white matter during an individual experiment is shown in Fig. 2. Here, passage of the electrical impulses is seen to result in an immediate increase in respiratory rate. On stopping the impulses respiration fell to about its original value. Unstimulated tissue had continued to respire at this rate through-

TABLE II.—*Increased Metabolic Activity of Human Cerebral Preparations on Electrical Stimulation.*

Values during stimulation are in italics, and in the case of respiration, rates are followed by the stimulating voltage in parentheses.

| Source of specimen. | Time between removal and commencement of metabolism (min.). | Portion examined. | Preparation of tissue. | Electrodes. | Respiratory rate (μmol./gm./hr.) during successive 30-min. periods. | | | | Lactic acid (μmol./gm./exp.). |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | 1st. | 2nd. | 3rd. | 4th. | |
| Left frontal region | 105 | Grey matter | Slices | Grid | 48 | 48 | 47 | 45 | 23 |
| ,, ,, ,, | 105 | ,, ,, | ,, | ,, | 57 | *84* (22) | *78* (13) | 60 | *68* |
| Right temporal lobe | 86 | ,, ,, | ,, | ,, | 45 | 45 | 48 | — | 44 |
| ,, ,, ,, | 86 | ,, ,, | ,, | ,, | 38 | *52* (18) | 33 | — | *62* |
| ,, ,, ,, | 86 | ,, ,, | ,, | ,, | 36 | *56* (16) | 33 | — | — |
| ,, ,, ,, | 86 | ,, ,, | ,, | ,, | 40 | 58 (12) | 36 | — | — |
| Left frontal region | 110 | (*a*) White and grey matter from cerebral hemisphere, in approximately equal amounts | Slice-fragments | Concentric | 26 | *38* (12) | *55* (24) | 33 | *76* |
| ,, ,, ,, | 84 | (*b*) As (*a*) but posterior to that specimen | Ditto | ,, | 26–30 | *45* (12) | *61* (24) | 31 | *99* |
| Right temporal lobe | 88 | Grey matter | Chopped | ,, | 43 | 43 | 43 | 43 | — |
| ,, ,, ,, | 88 | ,, ,, | ,, | ,, | 39 | *56* (12) | *56* (12) | 48 | — |
| ,, ,, ,, | 88 | ,, ,, | ,, | ,, | 40 | *64* (24) | *64* (24) | 47 | — |
| Temporal lobe | 70 | ,, ,, | ,, | ,, | 22 | 22 | 22 | 22 | 62 |
| ,, ,, | 70 | ,, ,, | ,, | ,, | 22 | *41* (12) | *45* (24) | 25 | *91* |
| ,, ,, | 70 | Subcortical white matter | ,, | ,, | 13·5 | *26* (2) | *29* (24) | 15 | *67* |

out the experiments. The increase occurred both with grey and with white matter. There was some difference in response with different voltages of the applied stimuli, and the highest rate observed was about twice the unstimulated value. Each of the rates was derived from some 6 sets of experimental observations, which provided the experimental points seen in Fig. 2 for each of these periods. The association of the increased respiration with the electrical stimulation is clear. The nature of the association, especially in relation to any artefacts arising from the passage of electrical pulses, has been examined carefully in experiments with tissues from lower animals (McIlwain, 1951*a*). In addition there were included periodically during the present investigations experiments in which the same stimulators, vessels and electrodes were used without any tissue. These experiments never showed progressive gas changes which might be mistaken for respiration.

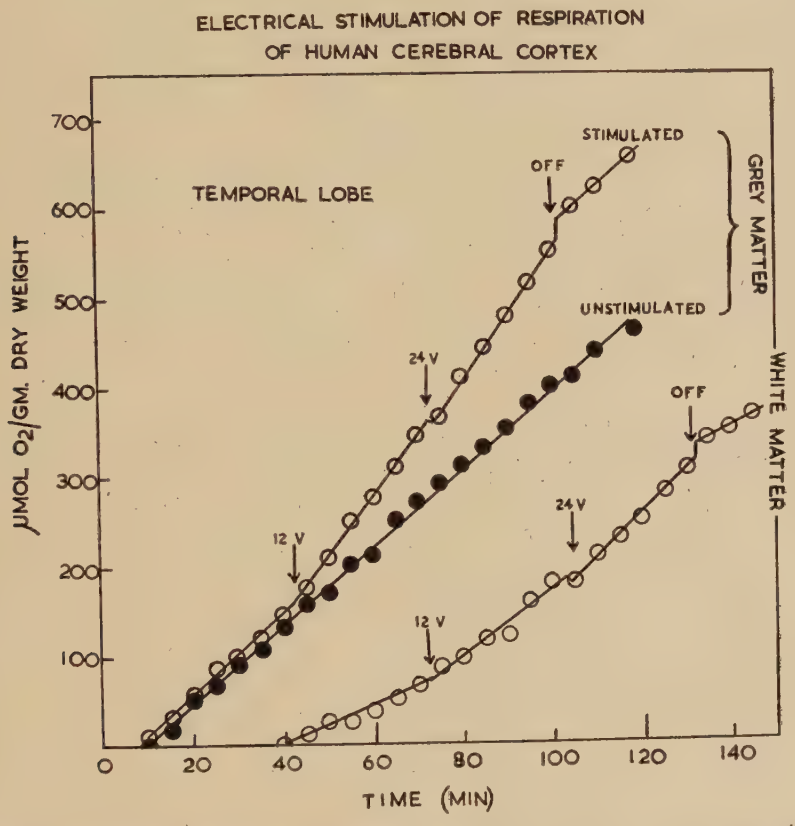


FIG. 2.—Respiratory response of chopped human cerebral cortex. Tissue was in vessels with concentric electrodes to which impulses of the characters described in Fig. 1 were applied.

Abscissa: time from commencing manometric experiment, with values for white matter increased by 30 min.

Further results are recorded in Table II. This gives data for respiratory rates of human cerebral tissues during some 52 experimental periods, of which 17 were during the passage of electrical impulses. The mean rate in the absence of impulses was 38 μmol./gm./hr., and in their presence, 56.

Lactic acid formation by human cerebral tissues was also increased by passage of electrical impulses. This again is indicated in Table II. The values quoted are not of rates, but of quantity of lactic acid formed during experiments in which the specimens have been exposed to stimuli for somewhat less than half the duration of the experiments. Minimum values for the increase in rate of lactic acid forma-

tion can be derived from the data (see McIlwain, Anguiano and Cheshire, 1951), and these indicate change in lactic acid formation to 2–3 times that of unstimulated value. Again, control experiments in the absence of tissue but with the vessels, electrodes, media and stimuli of the present experiments, showed no formation of substances which might appear as lactic acid by the method of estimation used.

## Discussion.

It is satisfactory to find that separated human cerebral tissues can be studied in an electrically stimulated condition by the present methods. In devising such methods in experiments with lower animals, conditions were in part derived from observations on man and other primates (McIlwain, 1951*a*) in relation to stimulation frequency, voltage gradient, duration of impulses, and the knowledge that greater electrical activity in the brain *in vivo* was associated with increased rates of metabolism.

In comparing the present results with those obtained with laboratory animals, it is seen that the maximal degree of respiratory response to stimulation is approximately the same in the two cases. The minimum potential gradient required for this has not been determined accurately with human material, but appears to be not very different from that in experimental animals.

The possible nature of the electrically-induced activity has been discussed elsewhere (McIlwain, 1951*a*, *c*). Results of applying the present methods to material from experimental animals lead one to expect that they should yield a variety of new types of information with respect to human tissues. With experimental animals, dependence of the response on the presence of particular substrates and other constituents in the surrounding fluids, and change in the response in the presence of added drugs, have already been demonstrated (McIlwain, 1951*d*; McIlwain, Anguiano and Cheshire, 1951; Gore, 1952). With human tissues there is the further major possibility that response may be altered by disease.

## Summary.

1. Respiration of small portions of human cerebral tissues has been measured in oxygenated nutrient salines. The respiratory rate of the specimens increased when suitable fluctuating potential gradients were applied to them. Responses were obtained in portions weighing 1–100 mg.

2. Respiration of grey matter from different areas, and also of white matter, approximately doubled in rate when up to 24 v. (peak potential) was applied as condenser pulses of time-constant 0·5 msec., 100 times/sec.

3. The rate of aerobic glycolysis also increased under these conditions.

4. Tissue specimens could be stored at 0° for at least 2 or 6 hours, and still responded to applied electrical stimuli when restored to good metabolic conditions.

We are greatly indebted to the Board of Governors of the Bethlem Royal Hospital and the Maudsley Hospital for a grant from the Research Fund which contributed to the expense of these investigations.

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# STUDIES IN LEARNING IMPAIRMENT. II: PSYCHONEUROTIC PATIENTS.

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In the first part of an experimental study of learning impairment (Hall and Crookes, 1951) the present writers described some of the distinctive features of the performance of schizophrenic and organic patients on two learning tasks. Brief reference, by way of introduction, was also made to studies of learning efficiency in psychoneurotic patients which were carried out by Zangwill (1943, 1946) and Trist (1941). These writers, and also Davis (unpublished), noted particularly some of the reactions and types of failure that neurotic patients sometimes show, with special reference to the Rey performance test. Certain reactions to the test were felt to be characteristic, for example, of patients with anxiety states or hysterical reactions, although none of the writers had carried these observations further or confirmed them experimentally.

In the present paper, therefore, we have made an attempt to follow up and verify these observations, in order to try and establish, at any rate in a preliminary way, (i) whether or not patients classed as psychoneurotic tend to be less efficient in learning than comparable normals, (ii) whether, as the previous writers contend, there are any characteristics of learning performance which are at all distinctive within the psychoneurotic group; for example, do anxiety cases show any difference from reactive depressives, obsessionals or hysterics, or are the variations that these writers observed merely general to the neurotic group as a whole?

## Learning Tasks.

To investigate this problem the same two tasks (one verbal, one performance) were used as for Part I of the experiment. A brief summary of these tasks is as follows:

(i) The verbal task consists of 10 pairs of words, which have to be learned so that, when only the first word of a pair is given following the reading through of the complete list by the experimenter, the patient can produce its correct associate. This procedure is repeated up to a maximum of 10 times, or until all the 10 pairs have been correctly recalled at any trial before the 10th.

(ii) The performance task consists of learning 5 different combinations of three two-way switches shown on a panel. Each of the correct combinations of the switches will turn on an electric bulb visible to the patient. Each move of the switches that the patient makes in carrying out the task is recorded on a chronograph, the patient being allowed up to a maximum of 10 trials to find out and learn to set these 5 combinations in the least possible number of moves.

Both tasks allow for some objective assessment of learning progress, together with opportunity for recording the qualitative features of a patient's performance.

## Clinical Material and Control Group.

The normal control subjects were the same for this experiment as for Part I of this investigation. The control group for the word-pair learning consisted of 32 subjects of both sexes, and that for the switch learning consisted of 26 subjects of the same group. A Wechsler vocabulary score was obtained for each subject. Age and vocabulary score distribution is similar to that of the psychoneurotic group, age range being from 17 to 46, average 29·0, although the average vocabulary score of 30·5 is slightly higher.

The psychoneurotic group consists of 71 patients of both sexes. The age range is the same as that for the normals (17 to 46). Clinically, some of the patients show a mixed symptomatology, but the subgrouping according to primary symptoms is shown in Table I, together with sex distribution, average age and average Wechsler vocabulary score for each of the 4 subgroups.

TABLE I.

| Primary symptoms. | Sex distribution. Male. | Female. | Total. | Average age. | Average vocabulary score. |
|---|---|---|---|---|---|
| Anxiety | 17 | 22 | 39 | 29·9 | 26·7 |
| Depression | 9 | 10 | 19 | 31·3 | 26·9 |
| Hysteria | 2 | 5 | 7 | 24·0 | 21·3 |
| Obsessional | 3 | 3 | 6 | 31·2 | 29·0 |
| Total | 31 | 40 | 71 | 29·8 | 26·4 |

Within the psychoneurotic group the hysterics are both younger and score lower on vocabulary than the normals and the other three neurotic groups. The two main neurotic groups, the anxiety and reactive depressive cases, show very little difference in either respect.

## RESULTS.

### 1. *Word-pair Learning.*

Performance of each patient on the word-pair task was analysed and scored in three different ways :

(i) Mean number of correct recalls per trial.

(ii) Lapses in score : this is the sum of the amounts by which the number of recalls on each trial falls below the level already reached on the preceding trial. For example, if a patient were to recall 6 word-pairs on trial 1, 8 on trial 2, 6 again on trial 3, thereafter maintaining or improving his score until the maximum was reached, his lapse score would be 2.

(iii) Forgetting index : this is found by obtaining the mean number of word-pairs forgotten per trial. For example, if a patient recalls correctly the word-pairs " old—easy," " general—small," " thought—comfort," on trial 1, then forgets two of these on trial 2, 3 of those that he recalled correctly on trial 2 at the third trial, but recalls all 10 correctly on trial 4, his forgetting index is 5 divided by 4 = 1·25.

By treating the results in this way, we find not only a considerable overall difference between normals and neurotics, but also various characteristics of performance or failure emerge from examination of results within the neurotic group itself.

#### (i) *Mean Correct Recalls.*

Comparison of the normal group with the whole neurotic group on this score shows that the former recall a much greater number of pairs. The means for the two groups are highly significantly different (the value of $t = 3{\cdot}984$, which gives a probability of chance occurrence of less than ·001).

The scores for the subgroups of neurotics are shown below, the abbreviations N = Normal, A = Anxiety, D = Depressive, H = Hysteric and O = Obsessional, being used in all subsequent tabulation of results.

| | N. | A. | D. | H. | O. |
|---|---|---|---|---|---|
| Mean number of correct recalls per trial | 8·48 | 6·98 | 7·08 | 6·37 | 7·12 |

Analysis of variance was applied to these data. The estimates of variance derived from the differences (i) between the five groups, and (ii) within the groups, give a variance ratio of 4·13, which gives a highly significant value of $P = < {\cdot}01$. Although the numbers of H and O patients are too small to allow of reliable conclusions, it is worth noting that the H patients are the worst and the O patients the best of the neurotic group.

This difference between the normal and neurotic groups is emphasized by consideration of the actual percentage of cases in each group who fail to reach a perfect score after the maximum 10 repetitions of the word-pairs. Only 12·5 per cent. N fail to reach maximum, as compared with 33·3 per cent. A and 36·9 per cent. D.

(ii) *Lapses in Score.*

The mean amount lapsed, together with the percentage of cases in each group who have no lapses at all, is shown below:

| | N. | A. | D. | H. | O. |
|---|---|---|---|---|---|
| Mean amount lapsed . . . | 0·56 | 1·31 | 1·63 | 2·14 | 1·50 |
| Percentage of cases with no lapses . . . . . | 72 | 44 | 42 | 14 | 67 |

With regard to the amount lapsed, the A group is closest to the normal, although all neurotic groups tend to be considerably poorer. The proportion of cases having no lapses to those with lapses is significantly different as between N and A, N and D, N and H, but not between N and O (values of $chi^2$ are: N and A — 5·72, N and D — 4·38, and N and H — 5·80, with corresponding probabilities of $< \cdot 02$, $< \cdot 05$ and $< \cdot 02$ respectively).

(iii) *Forgetting Index.*

The index for each of the five groups is as follows:

| N. | A. | D. | H. | O. |
|---|---|---|---|---|
| 0·45 | 0·56 | 0·59 | 0·51 | 0·53 |

All the neurotic groups have a higher average score than the normals, but analysis of variance yields a high value of P, so that little significance is to be attached to the differences. The differences between N and A and between N and D, considered separately by the *t* method, are not significant.

The general implication for the findings on the word-pair task seems to be that, although the neurotics are worse in learning the material than the normals, this is due not so much to any retention defect as to their inability to sustain the necessary effort throughout the task. Hence they show a very much greater tendency than the normals, not to forget what they have already learned, but to lapse below their previous level of attainment—as though their learning effort is typically less concentrated, more dispersed and superficial.

(iv) *Difference on Word-pair Learning between Males and Females.*

There is some evidence of differences in performance on this task between the male and female subjects. This is shown by the scores for N, A and D males and females given in Table II below.

TABLE II.

| | Mean correct recalls. | | Lapse score. | | Forgetting index. | |
|---|---|---|---|---|---|---|
| | M. | F. | M. | F. | M. | F. |
| N . . . | 7·86 | 9·02 | 1·00 | 0·18 | 0·55 | 0·34 |
| A . . . | 6·32 | 7·48 | 2·00 | 0·77 | 0·62 | 0·52 |
| D . . . | 7·53 | 6·67 | 1·00 | 2·20 | 0·43 | 0·74 |

From inspection of this Table it will be noted that the N and A females tend to do better than the males, while, on the other hand, the female D patients are *worse* than the males. The O patients show a similar trend on mean correct recalls, M being 7·53 to F 6·70. While no general significance can be attached to these observations without further confirmation, they may constitute at least one factor accounting for the inter-group variation.

*2. Switch Learning.*

Three different scores are also obtained for each subject on the switch-learning task. These are:

(i) Learning score: Mean number of switch combinations correctly recalled, and multiplied by 2 in order to be comparable with the equivalent score on word-pairs, both tasks having a maximum possible score of 10.

(ii) Trial and error scores: Two ways of scoring trial and error on this task have been used:

(*a*) The number of switch moves made by each individual on the 1st trial of the series, and—

(*b*) The mean number of moves required to reach each correct combination when this has not been correctly recalled.

(iii) Forgetting index: The mean number of switch combinations forgotten per trial.

In addition, (iv) the average time taken per move has been calculated.

(i) *Learning Score.*

Mean learning scores for the 5 groups are as follows:

| N. | A. | D. | H. | O. |
|---|---|---|---|---|
| 6·77 | 6·26 | 5·37 | 5·40 | 4·77 |

The difference between the means of the normal and the whole neurotic group is significant ($t = 2{\cdot}197$, $P = < {\cdot}05$). However, analysis of the variance between N, A and D, and between all 5 groups, shows that the between-group differences are not quite significant. The variance ratio for N, A and D is 2·44, with F just over ·05, while the variance ratio for all 5 groups is 2·19, which is still not quite significant. The difference between N and D separately is significant ($t = 2{\cdot}460$, $P = < {\cdot}02$).

(ii) *Trial and Error Scores.*

(*a*) The average number of moves made by each group on the 1st trial of the switch task, when the individual has to discover for himself by trial and error how the switch combinations occur, is as follows:

| N. | A. | D. | H. | O. |
|---|---|---|---|---|
| 25·46 | 34·0 | 39·2 | 28·9 | 40·0 |

It will be seen that all the neurotic groups have a higher average than the normals. While analysis of the variance between the 5 groups shows these differences to be not quite significant (V.R. = 1·70, $P = > {\cdot}05$), and separate comparison of N and A is just below the ·05 level, both D and O patients have a significantly greater number of moves than the normal (values of $t$ are 2·386 and 2·557, $P = {\cdot}02$ and less than ·02, for D and O respectively).

There is, therefore, a general trend for the neurotic patients to have an approach to the initial stage of the task that is less systematic and shows perhaps less appreciation of the limited possibilities of correct solution than the normal. This tendency is perhaps surprisingly marked in the obsessional patients, who show the highest number of moves of all the groups. The hysterics are nearest to the normals.

(*b*) The second kind of trial and error score provides some indication of the individual's reactions in the sequence and method of learning throughout the task. It was thought that this measure would serve a similar purpose to the lapse score in the word-pairs, indicating the capacity to sustain the learning effort. The mean scores for the 5 groups are:

| N. | A. | D. | H. | O. |
|---|---|---|---|---|
| 7·12 | 7·80 | 7·93 | 8·23 | 8·38 |

There is no significant difference between any single neurotic group and the normals. The obsessionals are again the worst.

(iii) *Forgetting Index.*

The mean value of the forgetting index for each of the 5 groups is as follows:

| N. | A. | D. | H. | O. |
|---|---|---|---|---|
| 0·44 | 0·51 | 0·58 | 0·60 | 0·52 |

Although there is a general tendency for the neurotics to show more forgetting than the normals, analysis of the variance shows that the difference is not significant. Separate comparison of D and H with N is almost significant at the ·05 level.

(iv) *Average Time per Move.*

Average times, in seconds, taken on each move are :

| N. | A. | D. | H. | O. |
|---|---|---|---|---|
| 2·41 | 2·10 | 2·99 | 2·17 | 2·09 |

Analysis of the variance between N, A and D is significant (variance ratio is 4·57, $P = < ·05$). The difference between A and D separately is significant, the D group being markedly slower than all the other 4 groups. The fact that the patients of the A, H and O groups all tend to make the switch moves quicker than the normals seems to indicate that their approach to the task, and their attitude towards solving it, is less deliberate.

A general summary of the findings on this switch-learning task seems to show that, whereas all the first three aspects of the learning performance show the normals to come out rather better than the neurotics, the differences between them are not so great as might have been expected. In all aspects of the performance the anxiety patients are nearer to the normals than the depressives. In fact, there is no statistically significant difference on any of the three measures, or in tempo of moves, between the anxiety group and normals. The depressives, on the other hand, are significantly worse than the normals on learning score and trial and error, and they tend to forget more than the normals. They are also, as was to be expected, considerably slower.

As far as the hysterics and obsessionals are concerned, the number of cases is too few to allow of any definite conclusion. Certain features of their performance are, however, quite suggestive, and might repay further study. For example, except on the forgetting scores, the hysterics learn rather surprisingly better than the obsessionals, having a much lower trial and error score, and a higher learning score. Although the average age of the hysterics is lower, their average intelligence is also lower ; so that there is a possibility that, on this task at any rate, some such feature as over-preoccupation may interfere considerably in the obsessional's learning progress.

(v) *Difference Between Sexes.*

As with the word-pair task, we find that there are certain differences between the performance of males and females within the clinical groups. Table III below shows the mean scores in each group of males and females taken separately. (The hysterics are not included, as there were only 2 male cases.)

TABLE III.

| | Learning scores. | | Trial and error scores. (*a*) | | (*b*) | | Forgetting index. | |
|---|---|---|---|---|---|---|---|---|
| | M. | F. | M. | F. | M. | F. | M. | F. |
| N | 6·39 | 7·27 | 23·5 | 28·2 | 6·58 | 7·86 | 0·52 | 0·34 |
| A | 6·21 | 6·30 | 33·4 | 34·5 | 7·52 | 8·02 | 0·53 | 0·51 |
| D | 6·40 | 4·44 | 32·4 | 45·2 | 7·62 | 8·20 | 0·52 | 0·64 |
| O | 4·73 | 4·80 | 36·7 | 43·3 | 8·47 | 8·30 | 0·57 | 0·47 |

It will be seen from these figures that in the normal group the females make a better learning score than the males, and have a lower forgetting index, but make a higher, that is, worse, trial and error score. This confirms the finding in the word-pair task that the females retain better than the males, but it suggests further that they are less good at finding the position when it is not retained, that is, at making a systematic elimination of the different possibilities.

In the anxiety group males and females are little different, but in the depressive group we find, as in the word-pairs, that the males are greatly superior in all the three scores.

If the three main groups only are considered, it will be seen that there is hardly any difference between the males in learning scores and forgetting index, so that almost all the variation between the clinical groups is due to the differences among the females, mainly the difference between normal and depressive females.

This inferiority of female depressives to both male depressives and the other females may, in part, be due to age (average of female depressives is 33·4, that of male depressives 29·0), but the possibility remains that in the females the depressive symptoms are more generalized, and thus cause a greater impairment of concentration and motivation required for carrying out tasks of this kind.

### 3. *Comparison of Performance on the Two Tasks.*

By comparing the learning scores on the two tasks for each subject, we can get some idea of the relative performance of each group on the different tasks. Every group makes a higher average score on the word-pairs than the switches. The mean differences between the scores (word-pair score minus switch score) are shown below :

| N. | A. | D. | H. | O. |
|---|---|---|---|---|
| 1·22 | 0·72 | 1·71 | 0·97 | 2·35 |

A higher value means a relatively better performance on word-pairs. Thus, compared with the normals, A and H are relatively better on switch-learning, D and O on the word-pairs.

The fact that all groups make a higher score on word-pairs does not necessarily mean that the word-pairs are easier, as the scores may not be comparable, but there is other evidence that the word-pairs are found less difficult, in the fact that a larger proportion of all groups fail to reach a correct solution on the switches, as indicated below :

| | | N. | A. | D. | H. | O. |
|---|---|---|---|---|---|---|
| Per cent. failures | Word-pairs | 12·5 | 33·3 | 36·9 | 42·9 | 50·0 |
| | Switches | 30·8 | 48·7 | 63·1 | 57·1 | 83·3 |

Thus it is strange that the anxiety group are relatively less impaired on the harder task, as emotion is thought to have a greater disturbing effect on more difficult processes.

There is a general tendency for females to be relatively better on the verbal task. Mean differences between the two scores (word-pair score minus switch score) for males and females separately are shown below :

| Normals. | | All neurotics. | | All subjects. | |
|---|---|---|---|---|---|
| M. | F. | M. | F. | M. | F. |
| 0·88 | 1·60 | 0·83 | 1·39 | 0·84 | 1·43 |

### General Summary and Comment on Both Tasks.

In almost all respects the anxiety cases come closest to the normals on these tasks. As a group they tend to do worse on both tasks than the normals, but this is due mainly to the poor performance of a few individuals. Even on what has been considered a neurotic characteristic, as measured by the *lapses* in performance on either task, we find that a few cases lapse very much more than the normal, but that the majority are little different in this respect. We can therefore conclude, in-so-far as our particular groups are concerned, that, whereas the emotional disturbance is great enough in some of these patients to make them differ markedly from the normal average and to make them show "neurotic" tendencies such as spoiling their performance, failing to sustain the necessary mental effort and initial progress, the majority are not significantly worse than the normal. This finding, confirmed statistically, indicates the need for caution in drawing any conclusion as to the learning inefficiency of such patients when compared with the normal. Some of the normals were themselves undoubtedly performing, particularly on the switch-learning task, below their optimum level of efficiency owing to a temporary situational anxiety.

The depressive patients, on the other hand, are significantly worse than the

normals in almost all respects, and they therefore also tend to be worse than the anxiety cases. They are slower on the switches, they show a marked and significant tendency to lapse in their performance on both tasks, and they tend to forget what they have learned. It is particularly striking in this group how the female patients are more impaired than the male. The emotional disturbance of the former seems to have involved their concentration, their motivation toward the task and the experimental situation in general, and consequently their attitude towards their own performance, more profoundly. This seems to confirm the clinical impression of these patients.

Our findings for the hysterics and obsessionals can be taken as merely suggestive, and as perhaps indicating possibilities for further experimental research. The obsessionals, although they have the highest average intelligence of all the neurotic subgroups, are surprisingly poor on the switch-learning task, there being a very marked discrepancy between their scores on this and on the word-pairs. Possibly the orderly and systematic approach required for good solution of this task is impeded by obsessional adherence to particular move sequences already worked out by the patient, so that any breakdown in sequence caused by failure on a combination which the patient thought he knew may make it difficult for the patient to revise his scheme of approach. This would appear to be a phenomenon closely similar to the " rigidity " of concept formation which Rapaport has observed in such patients carrying out the Vigotsky sorting test. This adjustment difficulty is also shown by the fact that the obsessionals have the highest trial and error score of all the groups.

The hysterics, in contrast to the obsessionals, have the poorest learning score on the word-pairs, and show the greatest number of lapses on this task. They have also the lowest average vocabulary score, so that this task is probably proportionately more difficult for them. They are nearest of all the neurotic groups to the normals on trial and error score—at the opposite extreme to the obsessionals —so that there seems to be here a difference of some significance in approach to this task, the hysterics appearing to adjust quite easily to the sequence of switch combinations, and to eliminate errors with little difficulty.

In answer to the two questions posed at the beginning of this paper, (i) there is evidence of reduced efficiency in the word-pair learning among psychoneurotic patients, but for the switch task the evidence is not very clear, and (ii) there are signs, which have been discussed, of qualitative and quantitative differences in performance among the sub-groups of psychoneurotic patients ; but the aetiology of these differences is confused by the relatively great sex differences which have been observed simultaneously, especially in the switch-learning.

In general, progressive tasks of the kind used in the present study seem to bring out quite clearly certain features of so-called learning efficiency which cannot be objectively assessed with standard tests. By scoring and recording various different aspects of the whole learning performance, it is possible to distinguish something of the characteristics, qualities and extent of the emotional interference with the cognitive process. Not only differences in actual learning, but in method of approach, in ability to sustain mental effort and to recover after failure, are of varying importance in the performance of the neurotic patients. Some features of the results require further experimental study and corroboration, and the observed differences between male and female patients should lead investigators in this field to be cautious in the conclusions they may draw from results obtained with mixed groups.

We wish to thank Dr. R. E. Hemphill, Medical Superintendent, Bristol Mental Hospitals, for making available to us the clinical material for this study, and for his generous encouragement of the work. We also wish to thank Mr. B. Babington-Smith, of the Institute of Experimental Psychology, Oxford, for his advice on the statistical treatment of the results.

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# THE PSYCHIATRIC ASPECTS OF TEMPORAL ARTERITIS.

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Temporal arteritis, also called giant cell arteritis, or cranial arteritis, was first described in 1932 by Horton and Magath. This syndrome is caused by a reversible inflammation of the cranial arteries, especially the temporal arteries (which are visibly inflamed), causing headache, mental and neurological disturbances as well as general toxic signs, and almost always occurring after the age of fifty-five years.

*Pathology.*—In the arteries involved there is a subacute inflammation of the adventitia and media with focal necrosis of the media, fragmentation and destruction of the internal elastic lamina with gross hypertrophy of the intima, often leading to occlusion of the vessel. In many cases giant cells are found in the media. Besides the cranial arteries other vessels are sometimes involved, e.g., the carotids (Scott and Maxwell 1941; Gilmour 1941), subclavian, coronary and femoral arteries (Cooke *et al.*, 1946), post-auricular (Dick and Freeman 1940).

*Aetiology* is unknown. There is no evidence of tuberculosis or syphilis. A low-grade bacterial or virus infection of the arteries has been postulated, but repeated bacteriological examinations of the biopsied arteries have failed to isolate any organisms. The predilection which the condition shows for the temporal and cranial arteries is unexplained.

## Symptomatology.

*Headache* is a constant feature, and may be present for months before any other symptoms or signs appear. The headache is situated mainly in the fronto-temporal regions, but may also be occipital or generalized. It commonly disturbs the patient's sleep. Pain in the jaws on chewing may occur, also pain in the ear and gums.

*Arteritis.*—In a typical case the appearances are unmistakable. The anterior branches of the temporal arteries on the forehead are prominent and tortuous; the skin over them is red and inflamed, and on palpation there is tenderness and absence of pulsation. The cervical glands are occasionally enlarged.

*General signs.*—Intermittent pyrexia up to 101° F. is a usual feature. The pulse and respiration rates are normal. Malaise, vomiting, loss of weight, anaemia, general weakness and tiredness, night sweats and joint pains may occur. The blood pressure is usually normal. Hypertension occurs in some cases, but probably no more frequently than would be expected in patients of the same age group.

*Blood examination.*—A high Erythrocytic Sedimentation Rate up to 100 mm. (Westergren) is always present, even in apyrexial periods, and may not return to normal until a considerable time after symptomatic cure (Robertson, 1947).

Blood culture is negative, as is the Wassermann reaction. An anaemia, probably toxic in origin, is frequent. The white cell count is generally normal, though a leucocytosis up to 20,000 per c.mm. does occur in some cases.

Pagliardi and Vitelli (1949) have drawn attention to the frequency of inversion of the albumin/globulin ratio of the serum in this condition.

## Mental Symptoms.

As this condition is essentially an affection of the cranial arteries, mental and neurological disturbances are to be expected.

*Depression* is the commonest presenting symptom in the prodromal period, often increasing in severity in the acuter phases of the illness. In some cases the depression may be partly due to the headaches, but in most cases it is mainly attributable to the cerebral arterial disease. In the case reported below the depression existed

for over eighteen months before the typical temporal signs appeared. Of the four cases described by Robertson (1947), three exhibited depression as a prominent feature. In Case 1 the face suggested profound dejection, which was confirmed in conversation. Case 2 was expressionless, dejected and ill-looking. Case 3 complained of general lassitude, depression and anorexia ; the only positive finding in her investigation on admission was a very high sedimentation rate. A patient of Chassnoff and Vorzimer (1944) became depressed, lost interest in herself and surroundings and refused to eat. Sprague and MacKenzie's (1940) patient manifested a period of great mental sluggishness. Wilson's (1949) patient recently had become tired and nervous. In the case reported by Andersen (1947), " during the entire course of the disease he had a tendency to weeping, and was on the whole psychically unstable in contrast with his previous habitus. Later he became anxious and depressed owing to his disease." This author says that the patients are often depressed, but that there are no reports of suicidal intentions. Kilbourne and Wolff (1946) report acknowledged irritability and retardation of thought in a patient.

Depression is characteristic of the earlier and milder degrees of the syndrome of temporal arteritis, and may be the only mental symptom exhibited during the entire course of the disease, but in the more acute stages there may be progression to confusion, delirium and coma.

*Confusion* is fairly common. In the case reported in this article the patient, a month after admission, became restless, grossly confused and completely disorientated as to time and place, often throwing off the bed-clothes and trying to get out of bed. In Case 3 of Cooke *et al.* (1946), on admission her mental powers were so poor that it proved difficult to get any consistent history, and the patient herself complained of increasing loss of memory ; later she was, for eight weeks, completely irrational, disorientated and at times delirious. Case 6 of the same authors was for a week mentally confused, incontinent of urine and faeces and had to be restrained from getting out of bed. The patient of Schaefer and Sanders (1942) became delirious, and the possibility of brain tumour with increased intracranial pressure was considered ; six weeks later the patient had made a remarkable recovery, being alert and free from symptoms. The patient of Bain (1938) was disorientated for a time but recovered completely. The patient may be " irrational for recurring periods " (Smith and Green, 1949). The patient of Curtis (1946) talked irrationally and obeyed commands poorly. The patient described by Dick (1948) a few days after admission became progressively more drowsy and disinterested in his surroundings, and slight mental confusion persisted for the next fourteen days.

*Hallucinations.*—It is presumed that hallucinations were present in the cases described above as being " delirious." Migone and Mortara (1949) report visual hallucinations of men and animals occurring in conjunction with a transitory hemiparesis in a case of temporal arteritis.

*Aggressive behaviour.*—A patient aged seventy-five reported by Kaye (1949) showed aggressive behaviour, particularly towards his wife, a few weeks before admission to hospital with temporal arteritis. His behaviour became normal three weeks after admission. However, he had always been of peculiar temperament and had two similar aggressive episodes previously, ten years and five years respectively before the present illness. The author did not feel that the psychiatric episode bore any relation to the temporal arteritis (personal communication). Aggressive behaviour has not been described in any other case of this condition.

Andersen (1947) and Brock and Ytrehus (1944) describe some of their patients as being " psychically unstable," but it is not clear what they mean by this.

## Neurological Features.

Neurological manifestations may appear singly or in combination, but they are less common than the mental manifestations.

*Ocular signs* occur in about 60 per cent. of cases (Wilson, 1949). The pupils may be unequal, or they may be dilated and show no reaction to light. Photophobia may occur. Scotomata, homonymous hemianopia and quadratic loss have all been reported. Papilloedema may occur, and in conjunction with other neurological and mental symptoms might lead to a diagnosis of intracranial tumour. Blindness, temporary or permanent may appear. Residual optic atrophy has been reported by Smith and Green (1949). In the majority of cases the ophthalmoscopic findings

have been trivial compared with the loss of function, and it is generally believed that the blindness is due to retinal ischaemia from involvement of the vessels behind the globe and out of range of opthalmoscopic examination (Harrison, 1948).

Oculomotor disturbances are occasionally present. Dick (1948) reports a case with slight bilateral ptosis and weakness of conjugate upward deviation of the eyes for one day. Murphy (1942) reports drooping of the left eyelid. Diplopia is rare.

Slight facial weakness has been reported in one case (Gilmour, 1941).

The auditory nerve is more frequently affected. A patient of Cooke *et al.* (1946) had attacks of vertigo and later became completely deaf for a time. Vertigo is also reported by Bowers (1940) and Murphy (1942), and tinnitus by Gilmour (1941) and Andersen (1947).

Temporary paralysis of the right 12th cranial nerve is reported in one case (Robertson, 1947).

Post and Sanders (1944) describe a patient who had periods of aphasia, memory defect and intermittent depression for two years previously, and who at examination showed smoothness of the face and lack of wrinkles suggestive of Parkinsonism but there was no tremor. Robertson (1947) also refers to the Parkinsonian appearance in two of his cases.

*An upper motor neurone lesion* of the limbs is reported in a few cases. The paresis was a temporary one in all cases. In a patient of Kaye (1949) the lower limbs were spastic and the plantar responses were extensor. In Case 2 of Robertson (1947) the right plantar response became extensor for about a week. A confusional state associated with paresis of the lower limbs is reported by Bourne (1947). Migone and Mortara (1949) describe hallucinations occurring in association with a transitory left-sided hemi-paresis.

*Apoplexy and coma* are more serious complications. Coma is of serious import but not always fatal, as Bowers (1940) and Migone and Mortara (1949) describe two cases with coma lasting for days and then recovery. A patient of Cooke *et al.* (1946) six weeks after discharge from hospital became drowsy and comatose and died within seventy two hours ; autopsy showed tiny softenings in the subcortical white matter and thrombosis of the related vessels. Chassnoff and Vorzimer (1944) ascribe the prolonged coma in their case to multiple cerebral thrombosis. Case 3 of Gilmour (1941) had cerebral infarction with haemorrhages in the pons and medulla and small infarcts in the anterior lobe of the pituitary. Case 2 of the same author developed a flaccid hemiplegia and died a few days later. Similar cases are reported by Curtis (1946) and Post and Sanders (1944).

Keen (1950) describes a case presenting as meningitis, with headache, photophobia, vomiting, pyrexia, neck rigidity, and the C.S.F. had a raised protein and globulin content.

*The cerebrospinal fluid.*—Of the cases in the literature where the C.S.F. was examined two-thirds were entirely normal, and one-third showed some abnormality, e.g., increase of albumin, globulin and cells (Gilmour, 1941 ; Migone and Mortara, 1949 ; Keen, 1950), and an abnormal colloidal gold curve in one case (Schaefer and Sanders, 1942).

*Course and prognosis.*—The average duration is six months, but some cases last up to thirty months. Remissions and exacerbations occur in some cases. The prognosis is good on the whole and most cases end in complete recovery. This is in contrast with most of the conditions for which temporal arteritis may be mistaken. Even severe cases with coma may recover completely. Occasionally residual disabilities may result, as in the patient of Sprague and MacKenzie (1940), who, after recovery, was considered by his intimates never to have fully recovered from his symptoms of lethargy and mental retardation. A similar result is reported by Curtis (1946). In the early years after this syndrome was first described emphasis was laid on the excellent prognosis, but more recently fatal cases have been reported, and Harrison (1948) has shown that in 21 per cent. of the cases described in the literature death occurred in association with the disease. Death may result from cerebral thrombosis or haemorrhage during the height of the disease, or from coronary thrombosis some time after apparent recovery (Kilbourne and Wolff, 1946 ; Cohen and Harrison, 1948).

*Diagnosis.*—The characteristic appearance of the temporal arteries with headache, mental symptoms, pyrexia and raised E.S.R. should suggest the diagnosis, which can be easily confirmed by biopsy of an inch of the affected temporal artery under local anaesthesia.

Polyarteritis nodosa is the condition which most resembles temporal arteritis from the pathological point of view, but clinically they are entirely separate conditions. Temporal arteritis occurs in much older patients, is characteristically most prominent in the temporal arteries and is less widespread in the viscera; the blood urea and kidney functions are normal; there are no aneurysms; the histological appearances are different and the prognosis is much better.

Thrombo-angiitis obliterans sometimes involves the intracranial vessels, but it differs pathologically and clinically from temporal arteritis. Cerebral arteriosclerosis does not cause pyrexia, raised E.S.R. or visible inflammation of the temporal arteries, nor does it undergo such dramatic improvement as commonly occurs in temporal arteritis. The same considerations apply to intracranial tumour.

The depression and retardation of temporal arteritis, especially in the early stages where a raised E.S.R. may be the only abnormal finding, may easily simulate ordinary melancholia.

The pyrexia, mental confusion and the protean neurological signs in temporal arteritis may cause a diagnosis of encephalitis to be made.

*Treatment.*—The best results have been obtained from biopsy of the temporal arteries (probably from the cutting of the sympathetic fibres to the arteries). Many other forms of treatment have been tried, but with varying results. Rice-Oxley and Cooke (1951) have recently reported good results in two cases from aureomycin.

## Case Report.

This report of a fatal case is of additional interest as, so far as I am aware, it is the first recorded case in the literature to have been admitted to a mental hospital.

William G.—, aged 67, was admitted on 17 February, 1950, as a voluntary patient to Tone Vale Hospital.

*Family history.*—Nothing relevant in any member of the family.

*Previous personality.*—He had always been quiet and reserved, even-tempered and reliable. He was always extremely clean and tidy in his person and liked a regular routine.

*Previous history.*—Quite healthy, mentally and physically, until two years ago, when he started getting heart attacks of an anginal nature, relieved by trinitrates. Then he began to feel depressed and miserable, spent half his time crying and expressed the hope that he would die soon. About six months before admission he complained of severe headaches, mainly in the left temporal region, and of severe earaches. For the two years previous to admission he had been under close supervision by his doctor, who could find no evidence of organic disease, apart from his anginal attacks.

*On admission* he looked dejected, with a tense drawn face and wrinkled brow. He complained of feeling increasingly depressed, especially in the past six months; he felt afraid and miserable and could not bear to be alone. He was worse at night, and slept badly because of the headaches. He did not appear unduly worried about his heart attacks. His actions, speech and thoughts were retarded. He did not exhibit agitation or apprehension. There was no evidence of delusions or hallucinations. Memory, orientation and intelligence appeared to be unimpaired.

Physical examination revealed nothing abnormal. His mental state seemed to be that of endogenous depression; E.C.T. was considered but was rejected because of the history of heart attacks. Because of these he was confined to bed and codeine tablets were prescribed for the headaches. Sodium amytal 6 gr. at night gave him some relief from his insomnia.

A week later he complained of more severe headache, and it was then noticed that the skin over the left temporal artery was red and inflamed. The left temporal artery was prominent, hard, showed no pulsation and was tender to touch. Questioning revealed that for some time past he could not lie on the left side of his face because of the tenderness, and because of this he always lay on the right side. There was also tenderness on palpation over both facial arteries and in the region of the occipital arteries. His temperature was now 99·2° F.; pulse and respiration rates were normal.

*Investigations.*—Chest X-ray was normal; heart not enlarged. Clinical examination of the heart did not reveal any gross lesion. Blood pressure was 150/95; no evidence of peripheral arteriosclerosis. Pulsation was present in both posterior tibial arteries; no evidence of thrombo-angiitis obliterans in the extremities. The central nervous system was essentially normal. The optic fundi showed no abnormalities; ear drums were normal. Antero-posterior and lateral X-rays of the skull were normal, and showed no evidence of calcification of the temporal or intracranial arteries. Nothing abnormal was found in the urine. Throat normal; edentulous.

Blood urea was 19·5 mgm. per cent.
Blood cholesterol was 194·4 mgm. per cent.
Blood W.R. and Kahn were negative.

Blood count showed a slight microcytic anaemia; white cell count was 6,000 per cmm.

E.S.R. (Westergren) was greatly raised ; 74 mm. in one hour ; repeated four days later it was 67 mm. in one hour.

Estimation of the serum protein showed inversion of the albumin/globulin ratio : Total protein = 6·04 gm. per cent.; albumin = 3·68 gm. per cent.; globulin = 3·26 gm. per cent.

*Progress.*– For the next two weeks there was fluctuation of the headache, of the depression and of the cutaneous reddening over the temporal artery. His temperature chart showed an intermittent pyrexia up to 101° F., with pulse-rate of 92 at times. He continued to complain of pains in his gums and ears. Biopsy of the temporal artery was considered, but was deferred because of his increasingly poor physical condition.

7 March : He was restless and rolling out of bed at night. The reddening of the skin over the left temporal artery became more noticeable.

14 March : He became very confused and disorientated, said the year was 1934. His speech was slurred and mumbling.

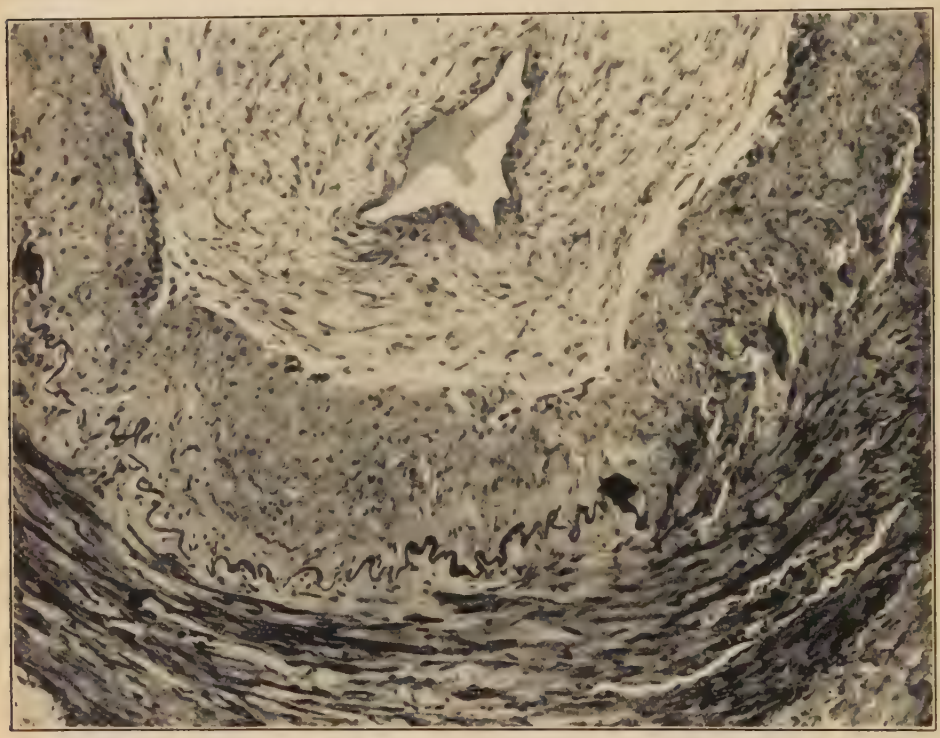

Fig. A.—Cross-section of left temporal artery showing clearly the destruction of the internal elastic lamina and the gross hypertrophy of the intima. The typical giant cells are not seen in this section. H. and E. × 150.

17 March : Still confused ; speech very slurred, restless and throwing back the bedclothes. Looked toxic, feeble and very miserable. He became incontinent of urine. Temperature rose to 101·6° F. and remained remittent up to his death twelve days later. His pulse was now 96 per min.

19 March : Difficulty in swallowing solids was noticed and he had to be put on a fluid diet.

22 March : Extremely confused and very restless, especially by night, continually trying to throw himself out of bed. Required sedation with paraldehyde orally.

27 March : Much feebler and more confused. The dysphagia had increased and he had difficulty in swallowing even fluids. Was now unable to speak, although he was conscious and tried to speak.

28 March : Lapsed into coma and died on 29 March

*Post-mortem examination* performed half-an-hour after death confirmed the diagnosis of temporal arteritis (Dr. A. M. Thomas, Pathologist, Musgrove Hospital, Taunton).

Lungs : Some slight terminal broncho-pneumonia.

Alimentary system : N.A.D. There was no lesion of the pharynx or oesophagus to account for the dysphagia.

Kidneys: N.A.D.

Cardiovascular system: In the heart there was a healed old infarct of the left ventricular wall. The coronary arteries showed sclerosis but were not occluded. The aorta showed some atheroma, with longitudinal wrinkling (also found by Sproule, 1942; and Gilmour, 1941).

The typical microscopic appearances of temporal arteritis (see Fig. A) were found in the temporal, cerebral, and superior thyroid arteries. No cerebral haemorrhage or infarction was found. No aneurysms were found in any vessels examined.

## Discussion.

The clinical and pathological features of this case are typical of temporal arteritis. The association of temporal arteritis and coronary artery disease present in this case has been repeatedly reported in the literature. The only feature in this case not previously reported is the dysphagia which occurred towards the end. This and the speech difficulty may have been due to involvement of the medulla.

The syndrome of temporal arteritis is comparatively uncommon (only about 130 cases have been reported since 1932), but several authors (Cooke *et al.*, 1946; Robertson, 1947; and Bourne, 1947) have pointed out that the condition is probably much more frequent than has been supposed. As nearly all cases exhibit some mental or neurological features its importance in psychiatric practice is obvious. If its existence is remembered the diagnosis in a developed case is easy. In the earlier stages the diagnosis is not so easy, but as an editorial in the *Lancet* (1949) points out, "It would, therefore, be wise to consider temporal arteritis as a possible diagnosis in any elderly patient with central nervous symptoms, especially when these are accompanied or preceded by a pyrexial phase." I would also like to point out that, in the earliest stages when there is no pyrexia and no definite physical findings, if temporal arteritis is suspected a high E.S.R. is very useful in strengthening one's suspicions.

## Summary.

The clinical features of the syndrome of temporal arteritis are briefly described and the mental and neurological features reviewed.

A case is reported, apparently the first recorded case in the literature to be admitted to a mental hospital or to come under psychiatric care for this condition.

## Acknowledgments.

I wish to thank Dr. K. C. Bailey, Medical Superintendent, Tone Vale Hospital, Taunton, for his interest and for permission to publish this case, and Dr. A. M. Thomas for the post-mortem examination and for the microphotograph.

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# AN INVESTIGATION OF THE ADRENOCORTICAL RESPONSE OF MENTAL PATIENTS TO E.C.T. AND INSULIN HYPOGLYCAEMIA.

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Somatic disturbances in schizophrenia include metabolic, circulatory and endocrine changes frequently associated with disorders of the pituitary gland and adrenal cortex. Depression of the metabolic rate is often severe (Hoskins, 1932), the systolic blood-pressure is sometimes as low as 80 mm. Hg (Hoskins, 1934; Rheingold, 1939; Shattock, 1950[1]), and the pulse pressure only a few millimetres. Peripheral vascular deficiency and atrophy of the tissues (Bleuler, 1920; Mapother, 1924; Minski, 1937; Shattock, 1950[1,2]), asthenia and various cutaneous changes are common; amenorrhoea is almost the rule.

It is remarkable that these disturbances are reversible, and that they are relieved or greatly alleviated during mental remission. Physical health is restored during a spontaneous remission, and a gradual improvement can be observed during a course of insulin comas. Sometimes a dramatic recovery follows electroconvulsion when this initiates a mental remission; somatic improvement is then rapid and the vascular deficiency may be relieved within a few hours (Shattock, 1950[1,2]). Unfortunately these remissions are often brief, and as relapses become more frequent after repeated treatment, physical and mental deterioration may be noticeable a few days after the initial improvement. The point of interest is a concordance of physical and mental changes, and not the therapeutic value of E.C.T. used as an adjunct to insulin treatment or as a means of moderating extreme restlessness in chronic patients.

Physical improvement following E.C.T. is often too rapid to be ascribed to favourable changes in a patient's general condition. Moreover, the same vascular recovery may occur in emaciated or well-nourished patients, in previously immobile or restless schizophrenics. A rise in the blood pressure—with improved peripheral circulation—is not related, in these patients, to intake of fluids or solid nourishment and physical exercise, or convulsions which are not followed by mental remission, do not promote this somatic recovery. Asthenia is relieved more gradually, and menstruation may be resumed in the early days of a remission or delayed indefinitely.

The somatic disturbances of schizophrenic patients, and their rapid reversal during a remission, suggest a functional pituitary and adrenocortical deficiency. This suggestion receives support from the observation (Shattock, 1950[1,2]) that an additional intake of sodium chloride or the administration of D.O.C.A. to chronic catatonic patients is sometimes followed by gratifying physical and mental improvement. The present investigation has been designed to ascertain whether E.C.T. and insulin hypoglycaemia owe part of their curative action to stimulation of the pituitary-adrenocortical system.

## Tests of Adrenocortical Function.

*Extracts from blood and urine.*—Many tests of adrenocortical function have been devised, none of them entirely satisfactory. Bornstein and Trewhella (1950) have described the assay of extracts from human plasma by Sayers' ascorbic acid depletion test; patients suffering from Cushing's syndrome showed greater activity, and cases of Simmonds' disease showed reduced activity. The rapid disappearance

of adrenocorticotrophic hormone from plasma and the difficulty of timing a rise in concentration of this hormone after E.C.T., added to other technical difficulties inherent in Bornstein's method, have not encouraged its use in this clinical investigation. Cope (1951) has elaborated another technique for detection of cortisone and 17-hydroxycorticosterone in urine and body fluids. This has yielded valuable comparative data, but only rough quantitative information (1951[2]), and has failed to demonstrate the presence of these substances in arterial and venous blood. Ashby (1949) investigated the excretion of cortical steroids in psychotic patients submitted to E.C.T. He found, in the majority of cases, a brisk outpouring of sugar-active and reducing cortins during the first days of treatment. In a later study of a case of periodic catatonia Ashby (1952) confirms the raised excretion of " sugar-active " cortins following E.C.T.

There is no general agreement on the accuracy of methods employed in the extraction of steroids from 24-hourly specimens of urine. These estimations can give only an indication of the effect of particular events or treatment on the total excretion of steroids. Seemingly trivial stimuli, such as venipuncture, which provoke cortical activity may obscure the importance of the stimulus under investigation. In psychotic patients there is the added difficulty of collecting 24-hourly specimens of urine.

*Changes in the number of circulating lymphocytes.*—Most observers agree that changes in the number of these cells are not a reliable index in man, whereas in some species of animal they are considered to give reliable information on cortical stimulation.

*Changes in the number of circulating eosinophils.*—Hills *et al.* (1948) have noted that the number of circulating eosinophils is dependent on the activity of the pituitary-adrenocortical system, and they have recorded a fall in the eosinophil count of normal subjects following injection of 25 mg. of ACTH. This observation has introduced a simple test, described by G. Sayers (1950) in a recent review of the subject, as probably the most useful index of adrenocortical function in man. We owe to Sayers (1948) the assay of ACTH in common use (the depletion of adrenal ascorbic acid), and his views on the eosinopenic test applied to man deserve our serious attention. The fall in the number of circulating eosinophils, four hours after administration of ACTH, is less variable and more considerable than the diminution in lymphocyte cells. A greater than 50 per cent. reduction after 25 mgm. ACTH is regarded by Thorn *et al.* (1948) as a " significant " eosinopenic response, although no statistical significance is implied. In Addisonian patients this response is absent, according to Thorn, but Sayers (1950) is more cautious. Although Sayers considers a satisfactory eosinopenic response to be " the first practical test of the functional capacity of the adrenal cortex in shock-like states," he emphasizes the importance of estimating the quantitative relationship between a stimulus and the response of the partially disabled glands of Addisonian patients.

A decrease in the number of circulating eosinophils is believed to be related to an increase in steroids oxygenated at $C_{11}$ and $C_{17}$. Speirs and Meyer (1949) have found that in adrenalectomized mice the eosinophil count is very sensitive to 11-oxysteroids and less sensitive to 11-desoxycorticosterone. Whereas ACTH causes an increase in all three cortical hormones, Thorn states that the increase in glucocorticoids only is detected by a reduction in the number of eosinophil cells.

Eosinopenia following ACTH, adrenaline, insulin, E.C.T., and various other stresses, has been recorded by numerous observers (Altschule *et al.*, 1949 ; Recant *et al.*, 1950 ; Kersley *et al.*, 1950 ; etc.), who regarded this response as an indication of adrenocortical stimulation in experimental and clinical work. Objections to this test have been raised, however, including the following :

(i) An eosinopenic response is observed when large doses of adrenaline are given to patients who suffer from Addison's disease. Recant *et al.* (1950) record these " unexpected responses," but attribute them to a survival of remnants of functional adrenal tissue. Positive responses do not occur in adrenalectomized dogs, and are absent in Addisonian patients after small doses of adrenaline or ACTH. A variable response to ACTH, particularly in Addison's disease, has been reported by Davidson (1951).

(ii) The eosinopenic response is unsatisfactory when heparin is given in adequate dosage. Eosinophilia persists in spite of administration

of ACTH (Godlowski, 1951), but this persistence may indicate only a positive balance between mobilization and withdrawal, or elimination, of eosinophil cells.

(iii) The most serious objection to the eosinopenic reaction is its dependence on a chain of physiological events. Its comparative simplicity may be misleading, but in the opinion of experienced workers it offers the best indication of adrenocortical responsiveness in man.

Clinicians have regarded changes in the " resting eosinophil level " as a measure of the therapeutic response to ACTH and cortisone treatment. A fall of this level, in patients who suffer from rheumatoid arthritis, is considered a favourable sign. If this reduction is not observed, when clinical improvement is evident, the eosinopenic test is condemned as an unreliable index of adrenocortical stimulation. But the test—as used by us—is confined to the comparison of counts made immediately before and four hours after adrenocortical stimulation, and when applied in this manner the value of the test has not seriously been questioned.

## Experimental Procedure.

*Collection of samples and counting of eosinophil cells.*—Samples of capillary blood were collected at the same time each day, the time being related to the patient's routine and the administration of E.C.T. or insulin treatment. Any change in daily routine was considered in relation to its possible effect on the eosinophil count. Practical details of the technique adopted were based on a preliminary investigation of technical and inherent distribution errors, so that cell counts which did not conform to the expected level of reliability could be discarded.

Blood was collected from the patient's thumb, in two standard pipettes, and eight serial counts by Randolph's technique (1949) were made in a B.S.S. counting chamber, type "A" ruling (Neubauer). From this the mean number of eosinophils per c.mm. of blood was calculated. Although Randolph's stain has proved satisfactory, we have found (as others have done) that its crystallization can be delayed by using a slightly higher dilution than was originally advocated.

The work of earlier observers is difficult to interpret. They did not always relate timing of the counts to the administration of physical treatment. Randolph (1950) has also pointed out that, when modifications of Dunger's eosin acetone diluent are used, it is necessary to fill the counting chamber within three minutes of the collection of each sample, in order to avoid a serious error in the count. This precaution can rarely be observed when samples are collected in the ward and examined in the laboratory. In the absence of these precautions the eosinophil count is not a reliable index of adrenocortical stimulation.

## Clinical Investigation.

Investigations were carried out on 72 mental patients (34 males and 38 females), of whom 40 were schizophrenics, 17 were suffering from an affective illness (15 depressives and 2 hypomanics), and 15 neurotic (anxiety, hysterical and obsessive) patients. Four hundred and sixty-four eosinophil counts were made on 68 patients.

*Preliminary investigation.*—This comprised twenty-one 2-hourly eosinophil counts, between the hours of 8 a.m. and 8 p.m., on 17 patients. Twelve counts, on days on which no physical treatment was given, showed great variability and only minor changes. Rud (1947), whose experience of eosinophil counts is probably unequalled, has noted the same lack of conformity in counts of different subjects. Nine 2-hourly counts, made on patients given E.C.T. at 10 a.m., showed a maximal fall at 2 p.m.—four hours after this treatment.

It was concluded that a comparison of two counts made at 10 a.m., immediately before E.C.T. was administered, and at 2 p.m., would give reliable information on a patient's eosinopenic reaction to a particular treatment.

*Eosinophil counts on control days.*—The counts of 40 patients on 50 days on which no physical treatment was given showed a tendency to a slight rise in the afternoon count. In 12 cases a more pronounced rise, and in 2 (a schizophrenic and a depressive) a fall greater than 50 per cent. The reason for this unexpected depression of the count is not known. It may be of interest to recall that three patients, not included in the present series, showed a similar fall after inhalation

of a minimal quantity of ether, and in one case after an emotional disturbance. These stresses are easily recognized, others may escape detection.

*Effect of E.C.T. on the eosinophil count.*—The 2 p.m. count of 37 patients, on 49 days on which E.C.T. was administered, showed in 31 cases (15 schizophrenics, 6 depressives and 10 neurotics) a fall greater than 50 per cent., and an occasional complete disappearance of eosinophil cells. In 12 cases (4 schizophrenics, 6 depressives and 2 neurotics) the afternoon count showed only an inconsiderable fall, in 6 others (1 schizophrenic, 2 depressives, 1 manic and 2 neurotics) an actual rise. An adequate eosinopenic response to E.C.T. was therefore lacking in approximately one-third of the total number of cases. Patients who failed to respond included 6 chronic schizophrenics who were sedated by E.C.T. but not otherwise benefited. Seven other chronic schizophrenics who also derived no benefit from this treatment showed, however, a depression greater than 50 per cent. in their afternoon count. Altschule (1949) has stated that the eosinopenic response is always adequate after a first electroconvulsive treatment, and that it may fail when repeated treatment is given at short intervals. Our results do not support his contention; responses were sometimes inadequate after first, second, third or later convulsions.

*Effect of insulin hypoglycaemia on the eosinophil count.*—A preliminary investigation was undertaken to determine the effect of insulin hypoglycaemia on the eosinophil count of schizophrenic patients. Fifteen observations were made on 8 patients who received coma doses of soluble insulin at 7 a.m. A sample of capillary blood was collected at the same time for a first eosinophil count. The second count, at 10 a.m. in 11 cases and at 11 a.m. in 4 cases, showed only minor and inconstant changes in all but one case, in which a rise of 45 per cent. was noted. The 2 p.m. count showed, however, in every case a considerable reduction in the number of eosinophil cells, a fall of 62–94 per cent. (mean fall, 74 per cent.) compared with the 10 a.m. count. It was concluded that comparison of 10 a.m. and 2 p.m. counts would give the required information on the patient's eosinopenic response to that treatment.

Twenty-seven of our patients, submitted to daily insulin hypoglycaemia, were investigated on 68 separate occasions. In every case where coma developed a significant fall in the eosinophil count was recorded at 2 p.m., 7 hours after injection of insulin and approximately 4 hours after the onset of coma. Seven patients (5 schizophrenics and 2 neurotics) who received only 10 to 50 units of insulin (mean value 20 units) developed no sopor or coma and only insignificant changes in the afternoon eosinophil count. A rise was present in five cases and an insignificant fall in two others.

Kersley *et al.* (1950) have found a maximal depression of the eosinophil count approximately 7 hours after insulin injection, in patients suffering from rheumatoid arthritis. This observation is in agreement with our findings after injection of greater doses of insulin. Kay and Thorley (1951) observed inconstant changes in eosinophil counts performed on a portion of resting and half-hourly blood samples taken from male schizophrenic patients undergoing insulin treatment. Three-and-a-half hours after injection of 4–24 units they noted a fall greater than 50 per cent. in 8 out of 10 cases, and after injection of 120–280 units a fall greater than 50 per cent. in 5 out of 9 cases. The technique adopted by Kay and Thorley differs in some important respects from that used in the present investigation. It seems probable that these differences would account for the early inconstant changes in the eosinophil count, noted by them 3½ hours after insulin injection. Withdrawal of venous blood at half-hourly intervals must provide additional emotional and physical adrenocortical stimuli which are absent in our cases. We have found, on the other hand, that observation over 6 or 7 hours is necessary to detect the characteristic late depression of the count, following insulin administration.

Hypoglycaemia is marked half-an-hour after injection of insulin. It is unlikely that it provides the direct stimulus for an eosinopenic reaction which is maximal 7 hours later, that is, 4 hours after cerebral changes attended by diminished awareness, sopor or coma. These changes may furnish the stimulus that liberates ACTH, induces an adrenocortical response and the consequent fall in the number of circulating eosinophils. Proof for this supposition is lacking, and it rests insecurely on the time-relation of these reactions. To ascertain whether glucose solution, given at 10.45 a.m. to interrupt coma, was responsible for the late reduction in the eosinophil count, the same quantity of glucose was given at the usual time to 6 patients from whom insulin was withheld. No fall in their 2 p.m. count was

observed, and it was concluded that this quantity of glucose is not the adrenocortical stimulus responsible for delayed eosinopenia.

*The "resting-level eosinophil count"* shows a gradual rise in many patients treated with insulin. This rise, reported by several observers (Rud, 1947; Sackler *et al.* 1951), has been confirmed by comparison of successive morning counts of a number of our patients. The rise was often considerable, the number of eosinophils being sometimes doubled and trebled during the second and succeeding weeks of treatment. It is not possible to say from our observations whether this rise is related to an eventual clinical improvement, as believed by Rud (1947) and also by Sackler *et al.* (1951).

The following investigations were undertaken to ascertain by indirect evidence whether eosinophil cells, which disappear from the peripheral circulation after E.C.T. or hypoglycaemic coma, are destroyed, or whether they are only temporarily withdrawn and stored in the tissues. A few interesting facts have emerged, but the question has only partly been answered.

(*a*) *Total leucocyte counts* on days when no physical treatment was given showed only minor variations throughout the day, but after E.C.T. a rise in the afternoon count was noted in many cases.

(*b*) *Differential leucocyte counts* showed, in some cases, a relative neutrophilia 4 hours after insulin coma, as compared with the pre-treatment count.

(*c*) *Cooke's neutrophil count* showed a marked shift to the left in the majority of cases examined, the number of immature granulocytes exceeding the accepted "upper normal limit."

(*d*) *Sternal marrow biopsies* were carried out on 6 patients who had previously received 20–60 coma doses of insulin. In 3 cases a slight rise in the number of eosinophil cells above the accepted "upper normal limit" was observed, and in the remaining 3 cases a relative increase in the number of immature eosinophil cells.

It was concluded on the above evidence that some at least of the eosinophil cells, which disappear from the peripheral circulation after adrenocortical stimulation, are destroyed or permanently withdrawn, and that the bone marrow is stimulated to increased activity by insulin hypoglycaemia.

## Discussion.

The therapeutic value of E.C.T. and insulin hypoglycaemia in the treatment of mental disease is generally recognized, but the mode of action of these physical remedies is still unknown, and we do not know why E.C.T. is more useful in the treatment of one mental illness and hypoglycaemia in that of another. Physical changes are common in schizophrenia, particularly in catatonia, but they are only striking during active phases of the illness. Relief of a disorder which suggests pituitary-adrenocortical dysfunction directs our attention to the effect of E.C.T. and repeated hypoglycaemia on the activity of the adrenal cortex.

The mental withdrawal of schizophrenic patients is facilitated by a diminution of physical responsiveness, depression of the metabolic rate and a fall in blood-pressure. Pincus *et al.* (1949), Parsons *et al.* (1949) and their associates have noted the inadequate adrenocortical response of schizophrenic patients to psychogenic and various environmental stresses, although their response to stronger stimuli, such as E.C.T., is usually adequate. Early *et al.* (1951) have noted that E.C.T. mobilizes large amounts of ACTH, and that the effect of one E.C.T. may be equivalent to a greater than 50 mgm. dose of ACTH.

The usefulness and limitations of the eosinopenic test, applied to patients undergoing treatment by E.C.T. and insulin, have been discussed, and a series of investigations are reported which prove insulin hypoglycaemia to be a reliable adrenocortical stimulus, and E.C.T. not so constant in its effect. The eosinopenic response is elicited by the liberation of oxycorticosteroids (Thorn *et al.*, 1948), which follows indirect stimulation of the adrenal cortex by E.C.T. and insulin hypoglycaemia. There is, however, no convincing evidence that these steroids, and particularly cortisone, possess therapeutic properties, and many disturbances of mental function have been reported after their administration to patients who suffer from rheumatoid arthritis. In two cases of "recurrent schizophrenia," studied by Rowntree and Kay (1952), a rise in sugar-active cortins was observed

during remissions and an increase in the electrolyte controlling factor at the onset of an attack. The physical signs of these patients were unusual, and in some important respects the converse of those generally encountered, and those observed in our cases. One of Rowntree and Kay's patients showed a rise in pulse rate, blood-pressure and pulse-pressure, flushing, sweating and a rise in temperature at the beginning of an attack (after the first signs of mental change), and a slower pulse and lower blood-pressure during remissions. The other patient showed less consistent clinical and biochemical abnormalities. The interest of a comparison with our cases lies in the demonstration of raised electrolyte controlling activity at the time the blood-pressure is higher, that is to say at the onset of an attack in their two patients, but at the time of a remission in ours.

If " sugar-active " cortins are not the only or main cortical steroids to be concerned in the improvement of the average case of schizophrenia, following adrenocortical stimulation, a positive eosinopenic reaction may only serve as an indication of more general cortical stimulation. Most workers are, however, agreed that retention of sodium and chlorine ions, similar to that induced by desoxycortone, follows the administration of ACTH (Morris, 1951). Bornstein and Gray (1951) also remind us that the so-called, " glycogenic hormones " affect sodium metabolism. A rigid subdivision into glyco- and mineralocorticoids is therefore undesirable, and the effect of ACTH liberation on mineral metabolism will depend on the relative proportion of steroids set free from the adrenal cortex and on their relative " electrolyte regulating " and " sugar-active " properties. The present study has supplied additional evidence of adrenocortical stimulation by two physical methods of treatment. Activation of the adrenal cortex, as revealed by the eosinopenic reaction, may explain the relief of physical disturbances which suggest an adrenocortical deficiency, although other possible and probable effects of these treatments are not excluded.

## Summary.

1. Clinical evidence in favour of adrenocortical dysfunction in schizophrenia and tests of adrenocortical activity are briefly reviewed.

2. The value of the eosinopenic test in man is discussed and the reasons for its adoption are stated. The technique adopted is described.

3. Four hundred and sixty-four eosinophil counts were made on 68 schizophrenic, affective and neurotic patients. A greater than 50 per cent. reduction in the total eosinophil count (by Randolph's method), 3–4 hrs. after stimulation, has been accepted as evidence of a satisfactory adrenocortical response.

4. Twenty-one 2-hourly counts, made on no-treatment days on 17 patients, showed only minor inconstant changes; comparison of the 10 a.m. and 2 p.m. counts of 40 patients, on 50 no-treatment days, showed no significant change.

5. A fall greater than 50 per cent. in the eosinophil count of 37 patients was noted, 4 hrs. after E.C.T., on 31 of 49 occasions on which this treatment was administered; no significant change was observed on 12, and a rise on 6 occasions. Depressive and neurotic patients failed to show a satisfactory response in one-half, and schizophrenics in one-third of the cases.

6. A fall greater than 50 per cent. in the eosinophil count of 27 patients was noted 7 hrs. after insulin injection on every one of 61 occasions when coma developed, but not on 7 occasions when only 10–50 units of insulin were given and the patient experienced neither sopor nor coma.

7. A rise in the resting-level eosinophil count after repeated insulin hypoglycaemia treatment, a left shift in the neutrophil count and evidence of bone-marrow activation suggest replacement of eosinophil cells, rather than temporary storage after adrenocortical stimulation.

8. The bearing of these observations on the treatment of schizophrenic patients is discussed.

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# THE EFFECT OF SEX HORMONES IN OLIGOPHRENIA

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The intelligence, as measured by standard tests, ceases growing after about 14 or 16 years of age, and slowly decreases from about 25 or 30 years of age (Wechsler, 1945). The sex glands are developing as the intelligence ceases to develop.

In view of these observations, consideration was given to the possibility that the defective developed mentally to a degree below the normal because too great a quantity of the appropriate sex hormones was circulating in the blood stream. In consequence, the opposite hormone was administered, stilboestral being given to males and pernandren to females.

## The Treatment and Results.

(1) *Boys*.—Stilboestrol was given to four young boys :

Case 1.—Aged 9 years. A dull imbecile not greatly interested in his surroundings or pictures. Behaviour good ; nocturnal enuresis present. He feeds, dresses and washes himself with supervision. Social age, 3·4 years ; social quotient, 38.

Treatment :

| | | | | | |
|---|---|---|---|---|---|
| ·12 | mgm. | stilboestral | *o.m.* | for 9 | days. |
| ·25 | ,, | ,, | ,, | ,, 5 | ,, |
| ,, | ,, | ,, | *b.d.* | ,, 14 | ,, |
| ,, | ,, | ,, | *t.d.s.* | ,, 19 | ,, |

No change occurred until the 6th week of treatment when he was noticed to be brighter and quicker in his movements. The following week he played more and became still brighter. This condition persisted to the end of the treatment, ten weeks after its commencement. S.Q. after treatment rose to 42.

Case 2.—Aged 11 years. A feeble-minded boy unable to count beyond 5, unable to read and unable to tell the time correctly. Unstable and irritable, but attends to his own needs. A constant masturbator. Social age, 5·6 years ; social quotient, 56. Mental age, 6 years ; intelligence quotient, 54·5.

Treatment as Case 1, but ·25 mgm. *t.d.s.* for 14 days, then ·25 mgm. *o.m.* for 6 days.

Six weeks after the beginning of treatment his agitation was less, he understood more readily and his speech difficulty had improved. In the following week he was quieter in school and his work was neater. The treatment was then stopped, but the improvement was maintained, the boy remaining more affable and a better worker. The mental improvement in this case may have been related to cessation of frequent masturbation. The I.Q. rose to 68 at the end of treatment, falling to 46 four weeks after the cessation of the treatment. The S.Q. rose to 59 and, three weeks after the termination of the treatment to 62.

Case 3.—Aged 11 years. A feeble-minded boy unable to count beyond 3 and able to read a few short words only. Unable to tell the time. He is a bully. Attends to his own needs and is clean. Social age, 7 years ; social quotient, 63. Mental age, 5 years ; intelligence quotient, 45.

Treatment as Case 1, but ·25 mgm. *t.d.s.* for 16 days, then ·25 mgm. *o.m.* for 3 days.

A slight increase in activity occurred during the fifth week of treatment. This became more definite in the week following, and in the 7th week improvement in concentration was observed. He became more interested and more attentive at school. His memory improved. The improvement persisted until 4 weeks after the cessation of treatment, when concentration deteriorated. His mischievousness returned in the 5th week. The I.Q. rose to 54·5 after treatment and remained at this figure. The S.Q. fell to 49, rising to 54·5 three weeks after the end of the treatment.

Case 4.—Aged 13 years. A bad-tempered, spiteful imbecile unable to count above 4. Mischievous and strikes others. Attends to his own needs and is clean. Social age, 4·6 years ; social quotient, 38.

Treatment as Case 1, then ·25 *o.m.* for 7 days.

The over-activity decreased and the outbursts of violent temper became less frequent 6 weeks after the beginning of the treatment. In the 7th week he was calmer and remained so until the 4th week after the cessation of the treatment, when he again became excitable. and talkative. In the week following, his bad temper and noisiness returned. The S.Q. fell to 36, rising to 40 two weeks after the cessation of treatment.

(2) *Youths.*—Stilboestrol was given to 7 youths :

Case (*a*).—Aged 15 years. Feeble-minded ; simple and inadequate. Unable to read or tell the time. Unable to perform calculations such as 1*s.* 8*d.* from 2*s.* 6*d.* M.A. 9·5 years ; I.Q. 68. S.A. = 15 years ; S.Q. = 100.

Treatment :

·25 mgm. *o.m.* for 21 days.
,, ,, alternate mornings for 21 days.

Two weeks after the commencement of treatment he had become less sullen and was a better worker, but by the end of the third week he had become noisy and insolent. At the end of the sixth week he was still defiant at times, although the stilboestral had been given on alternate days for 3 weeks. One week after the cessation of the stilboestral he looked calmer and was not defiant or troublesome. He remained in this state, although more settled than before the beginning of the treatment.

Case (*b*).—Aged 16 years. Feeble-minded ; immature and childish. Unable to read words longer than 3 letters. M.A. 10 years ; I.Q. 71. S.A. = 14 years ; S.Q. = 90.

Treatment as Case (*a*).

During the second and third weeks of treatment he became mischievous. Three weeks later he was more quarrelsome and interfering. One week after the cessation of the stilboestral he was more settled and was talking less indistinctly. The improvement in the speech continued and he returned to the mental state in existence before the beginning of treatment.

Case (*c*).—Aged 16 years. Feeble-minded ; dull and slow. Unable to read words longer than 3 letters, count 4 fingers, or subtract 4*d.* from 8*d.* M.A. 9 years ; I.Q. 64. S.A. = 10 years ; S.Q. = 62.

Treatment :

·25 mgm. *o.m.* for 21 days.
,, ,, *b.d.* ,, 7 ,,
,, ,, *o.m.* ,, 14 ,,
,, ,, *b.d.* ,, 21 ,,
,, ,, *t.d.s.* ,, 28 ,,

In the ninth week of treatment he became more active and in the following week he was noticed to be brighter mentally. Two weeks later, that is, in the twelfth week, the brightness had become more marked. After the cessation of the treatment his greater activity decreased, but he remained brighter than before the beginning of treatment.

Case (*d*).—Aged 17 years. Feeble-minded ; simple and easily led. Unable to read words longer than 5 letters. M.A. 11 years ; I.Q. 78. S.A. = 9 years ; S.Q. = 52.

Treatment :

·25 mgm. *o.m.* for 21 days.
,, ,, alternate mornings for 35 days.

By the second week of treatment he had become mischievous and noisy, and by the end of the third week was more mischievous. The stilboestral was reduced to alternate days and within a week he was behaving better. He again became quiet and orderly in his behaviour and remained so until the termination of treatment, which was stopped on account of homosexual activities, not hitherto observed. Three months after the cessation of treatment he had returned to the pre-treatment state.

Case (*e*).—Aged 17 years. Imbecile ; quarrelsome, impulsive and aggressive. Unable to read, tell the time or count above 4. M.A. 7 years ; I.Q. 50. S.A. = 4·3 years ; S.Q. = 24.

Treatment :

·25 mgm. *o.m.* for 14 days.
,, ,, alternate mornings for 7 days.
,, ,, twice weekly for 7 days.
,, ,, once ,, ,, 14 ,,

During the second week of treatment he became aggressive and impulsive and began to give orders to others. He remained domineering and, in the fourth week, smashed two

windows. Two weeks later he smashed another window. He remained brighter in appearance 2 weeks after the cessation of the stilboestral but 3 months later the condition before treatment had recurred.

Case (*f*).—Aged 19 years. Feeble-minded; dull. Unable to read or tell the time. M.A. 8·5 years; I.Q. 61. S.A. = 7 years; S.Q. = 36·5.

Treatment:

·25 mgm. *o.m.* for 21 days.
,, ,, *b.d.* ,, 21 ,,
,, ,, *t.d.s.* ,, 35 ,,
·5 ,, *o.m.* + ·25 mgm., midday and evening for 7 days.
,, ,, *t.d.s.* for 7 days.

During eleven weeks of treatment no mental change was observed. The stilboestral was stopped in the eleventh week owing to enlargement of the breasts. No mental change occurred after the cessation of treatment.

Case (*g*).—Aged 19 years. Feeble-minded; immature and simple. Unable to read, tell the time, or subtract 4*d.* from 6*d.* M.A. 8 years; I.Q. 57. S.A. = 10·5 years; S.Q. = 56.

Treatment:

·25 mgm. *o.m.* for 42 days.
,, ,, *b.d.* ,, 14 ,,
,, ,, *o.m.* ,, 7 ,,

Three weeks after the beginning of the treatment he spoke more freely and his enunciation was clearer. In the following week he was excitable and restless. One week later he was still restless and was irritable and much more active. A few weeks after the cessation of the stilboestral he lost his over-activity and became calmer again.

(3) *Girls.*—Perandren was given to 3 girls:

Case A.—Aged 15 years. Feeble-minded; immature and simple. Unable to read words longer than 4 letters or to tell the time accurately. Behaves well. Attends to own needs. M.A. 5 years; I.Q. 35·7. S.A. = 9·3 years; S.Q. = 62.

Treatment:

5 mgm. perandren linguets *o.m.* for 14 days.
10 ,, ,, ,, *o.m.* ,, 12 ,,
,, ,, ,, ,, *b.d.* ,, 13 ,,
5 ,, ,, ,, ,, ,, 10 ,,
2½ ,, ,, ,, *o.m.* ,, 14 ,,

Six weeks after beginning treatment, she was less over-active and a "swagger" in her walk became less marked. The following week she was more settled in school. A week later she was considered duller than before the commencement of treatment. No further change occurred until after the cessation of the perandren when she became brighter and more alert. The "swagger" again became marked.

Case B.—Aged 15 years. Feeble-minded. Unable to read, tell the time or count above 5. Occasionally hot-tempered. S.A. = 8·6 years; S.Q. = 57.

Treatment:

5 mgm. perandren linguets *o.m.* for 21 days.
10 ,, ,, ,, ,, ,, 6 ,,
,, ,, ,, ,, *b.d.* ,, 13 ,,
5 ,, ,, ,, ,, ,, 7 ,,
2½ ,, ,, ,, *o.m.* ,, 17 ,,

Two weeks after beginning treatment she was less noisy and remained less excitable until menstruation occurred 12 days early, six weeks after the first dose of perandren. She then became excitable. Two weeks later she was definitely dull and remained so until after the cessation of treatment when she became brighter.

Case C.—Aged 18 years. Imbecile. Seldom talks, but smiles fatuously. Unable to read or tell the time. S.A. = 2·9 years; S.Q. = 16·1.

Treatment:

5 mgm. pernandren linguets *o.m.* for 16 days.
10 ,, ,, ,, ,, ,, 12 ,,
,, ,, ,, ,, *b.d.* ,, 7 ,,
5 ,, ,, ,, ,, ,, 10 ,,
2½ ,, ,, ,, *o.m.* ,, 3 ,,

No mental change was observed until eight weeks from the beginning of treatment. She was then noticed to be duller than before the treatment was given.

The quantities recorded above for Cases A, B and C were not given consecutively. The intermissions were caused by Cases A and C vomiting before the first menstrual periods occurring after the beginning of treatment. In consequence the perandren was stopped about one week before each period was expected, and was not re-commenced until 3 days after the termination of each menstrual flow.

## General Observations.

### A. *Physical Changes.*

(i) *Weight.*—A study of the monthly weights of all the cases showed that no consistent rise or fall of weight took place during the treatment. Amongst the 4 young boys, the weight rose in 2, remained stationary in 1, and fell in 1 during the 3 months' treatment. In the 7 youths it rose in 3 and fell in 4, whilst in the 3 females it rose in 1, remained stationary in 1 and fell in 1. All changes were small.

(ii) *Menstruation.*—Two of the three females vomited at the beginning of menstruation whilst receiving 10 mgm. of pernandren *b.d.* Case A began a period 7 days early; Case B began 12 days early and Case C, 14 days early. Case C vomited more than once on this occasion. Whilst receiving 2 mgm. *o.m.* a menstrual period began 10 days early in Case A. All three cases had shown regular monthly cycles without vomiting previous to the administration of the pernandren.

(iii) *Nipples and breasts.*—Enlargement of these structures occurred in the male cases, after 23·58 mgm. had been taken in Case 1; after 19·83 mgm. in Case 2; after 21·3 mgm. in Case 3 and after 25·33 mgm. in Case 4. Amongst the youths, Cases (*e*) and (*f*) were the only patients to show enlargement of the breasts. In Case (*e*) enlargement took place after 38 mgm. and in Case (*f*) after 41·5 mgm. Greater quantities of stilboestral could be taken in these older cases, aged 16 and 19 years respectively, before enlargement of the breasts was observed than in the young boys, aged 9, 11, 11 and 13 years.

(iv) *Growth of beard.*—No change was observed in the growth of beard in the 7 youths except in Cases (*d*) and (*g*). The first, who required shaving twice weekly before the administration of stilboestral was begun, did not require shaving for 2 weeks consecutively during the second month of treatment. The second case, who also required shaving twice weekly before the commencement of treatment, needed shaving only once a week or even less, during the second month of treatment.

### B. *Mental Changes.*

The most important changes observed were a greater mental activity, with aggressiveness in some cases, in the males and dulling of the mental processes in the females. These alterations persisted during the treatment and passed away after the cessation of treatment. Table I demonstrates a tendency for the I.Q. to rise during treatment and for the S.Q. to fall, a total of 7 rises and 2 falls occurring in the I.Q. and of 4 rises and 0 falls in the S.Q. At the termination of the treatment the I.Q.'s. showed rises of from 7 to 14 points and falls of 4 points in magnitude. From 2 to 4 months after the cessation of treatment 4 further rises and 2 falls had occurred. These figures are well within the maximum variations previously reported as occurring on re-test but without treatment (Rudolf, 1949). The rises numbered 75 and the falls 41, and of the 75 rises of I.Q., 7 showed variations between 21 and 25 points. Of the 41 decreases, 3 showed figures of from 16 to 20 points.

With regard to the social ages an equal number, 14, of rises and of falls occurred during and after treatment. Table I demonstrates the variations in Social Quotients, and comparison of the social ages showed that 10 of the rises were below ·6 years in magnitude and 11 of the falls below 2·1 years in variation. The greatest rise was in the 3·6–4·0 group and the greatest fall was 11·2 years. These figures resembled those of variations in untreated cases, where 3 of 145 rises and 3 of 98 falls occurred in the 4·6–11·2 group.

In view of these considerations, no evidence exists that the treatment affected either the intelligence quotient or the social age.

TABLE I.—*Intelligence and Social Quotients.*

| Case. | Age. | I. | II. | III. | IV. | V. | VI. |
|---|---|---|---|---|---|---|---|
| 1 | 9 | — | — | — | 38 | 41 | 42 |
| 2 | 11 | 54 | 68 | 46 | 56 | 59 | 62 |
| 3 | 11 | 45 | 54 | 54 | 63 | 49 | 54 |
| 4 | 13 | — | — | — | 38 | 36 | 40 |
| (*a*) | 15 | 68 | 64 | 68 | 100 | 72 | 66 |
| (*b*) | 16 | 71 | 78 | — | 90 | 46 | 62 |
| (*c*) | 16 | 64 | 75 | 71 | 62 | 46 | 39 |
| (*d*) | 17 | 78 | 85 | 96 | 52 | 55 | 65 |
| (*e*) | 17 | 50 | 46 | — | 24 | 47 | 43 |
| (*f*) | 19 | 61 | 72 | — | 36 | 29 | 32 |
| (*g*) | 19 | 57 | 64 | 77 | 56 | 59 | 55 |
| A | 15 | 36 | 36 | 37 | 62 | 59 | 46 |
| B | 15 | — | — | — | 57 | 44 | 46 |
| C | 18 | — | — | — | 16 | 15 | 21 |

I = I.Q. before treatment; II = I.Q. immediately after end of treatment; III = I.Q. from 2 to 4 months after end of treatment. IV, V, VI = corresponding figures for Social Quotients.


## SUMMARY.

During treatment with stilboestrol in the males and perandren in the females a mental change took place in 13 of 14 cases treated. In males from 9 years to 19 years of age a greater cerebral activity, often with aggressiveness, occurred. All of 3 females, from 15 years to 18 years of age, became duller. During treatment a greater proportion of I.Q.'s. rose than fell. The opposite took place in the Social Quotients, the numbers of increases rising again within 3 months of the cessation of treatment. Comparison of these changes with those previously reported in cases untreated shows that these variations are within the limits of variation taking place on re-test in the untreated defective.

Owing to certain physical effects, namely menstrual vomiting with reduced inter-menstrual periods in the females, and increased development of breasts in the males, the treatment could be of a temporary nature only.

Within a few weeks of the cessation of treatment the mental condition had, except in a few characteristics, reverted to the pre-treatment state.


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# THE RELATION OF LATERALITY OF LESION TO PERFORMANCE ON WEIGL'S SORTING TEST.

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The Colour-Form Sorting Test was described by Weigl (1927) as one of a series of investigations into the nature of the psychological deficit resulting from a cerebral lesion. The material consists of 12 pieces: four squares, coloured severally red, yellow, blue and green; four circles, similarly coloured; and four equilateral triangles, similarly coloured (Fig. 1). They are presented in a random arrangement to the patient, who is asked to group them according to any similarity he sees; and when he has sorted them according to one principle, is then asked to sort them according to another.

Other problems involving sorting were presented in Weigl's study, and have been used in a number of investigations, particularly of the effects of frontal lobe lesions. Rylander (1939) found that his group of patients with frontal lesions differed significantly from the normal controls in the number of principles found for grouping 15 objects. Halstead (1940) used 62 common objects, and also found that patients with frontal lesions tended to find fewer principles for sorting than did patients with cerebral lesions located elsewhere. Subsequently Halstead and Settlage (1943) developed a mechanized grouping test, using geometrical figures: three patients, with frontal lesions, and one with a left occipital lesion, made many more errors than did the normal controls; while a patient with a right occipital lobectomy and one with a left parietotemporal lesion performed normally in this respect. Finally Halstead (1947) found that, of his group of "indicators" of cerebral damage, a similar test (No. 2) not only differentiated reliably the patients with cerebral lesions from the normal controls, but also gave a significantly higher error score with cases of frontal lesion.

Goldstein and Scheerer (1941) included Weigl's test in their experimental study of abstract and concrete behaviour; and Trist and Trist (1943) and Brody (1943) noted impairment on this test in cases of general paralysis and the presenile dementias.

The Colour-Form Sorting Test was originally designed, according to Weigl, to study the disabilities shown by aphasic patients in sorting coloured wools. Its use, however, demonstrated that the crucial problem involved, and one which the patient with a cerebral lesion could not overcome, was the necessity of shifting from one principle of sorting to another. The use of other sorting tests, providing many different principles for grouping, has confirmed this point; but the colour-form test provides a setting for the problem reduced to a minimum—only one "shift" being required for its solution.

The ability to shift from one principle to another involves the ability to *abstract* from the pieces presented their "common partial contents" of shape and colour, and to use these as the bases for two ways of grouping the pieces. It is a fundamental tenet of the Goldstein school that the underlying disability produced by a cerebral lesion is loss of this activity to assume an "abstract" attitude, leaving the patient able to utilize only a "concrete" approach to problems. Abstract and concrete attitudes, say Goldstein and Scheerer (1941), are "capacity levels of the total personality. Each one furnishes the basis for all performances pertaining to a specific plane of activity"; and, in considering the loss of ability to assume an abstract attitude, "we are dealing with a basic personality change."

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Such a widespread effect is not the consequence of a lesion of any particular location, it is simply the effect of " dedifferentiation of brain function " (Goldstein, 1948, p. 119) ; and in fact Goldstein and Scheerer do not mention the site of lesion in any of the cases described in their monograph. Weigl's study of the effect of cerebral injury was carried out, for the greater part, on a patient with bilateral frontal lesions ; and while other studies of performance on sorting tests have demonstrated greater impairment with cases of frontal lesion, none of the authors have noted any difference related to laterality of the lesion.

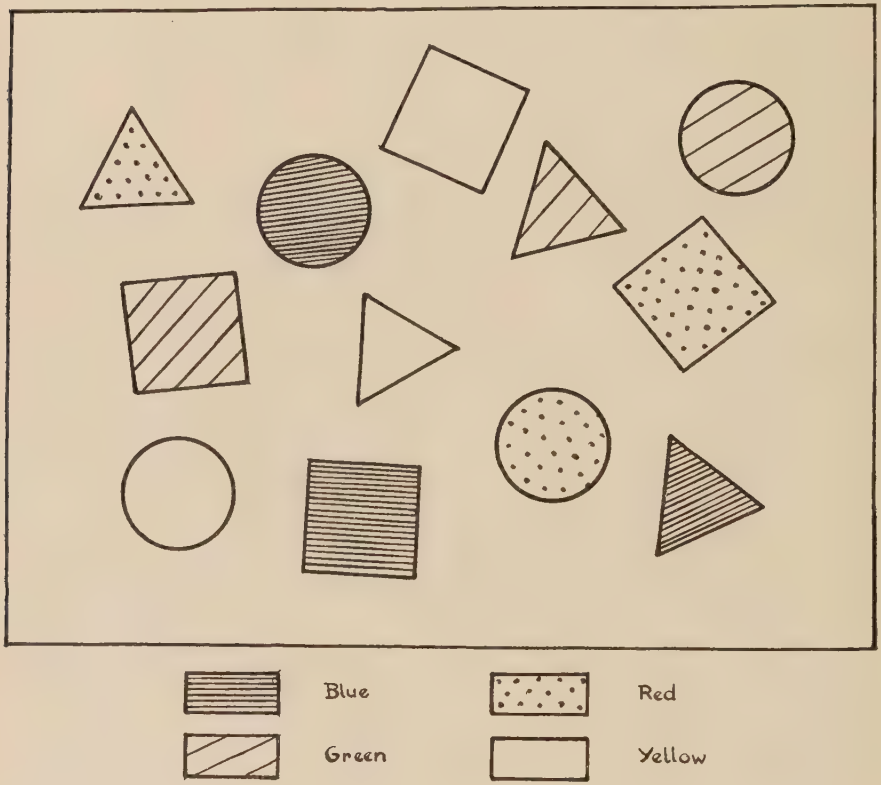


FIG. 1.

The results presented by Rylander (1939) and by Halstead (1940) show no significant difference between right- and left-sided lesions. In connection with the present study it is, however, noteworthy that of the three patients of Halstead and Settlage (1943) with frontal lesions, two had left-sided lesions, and the other, with a right-sided lesion, was left-handed. The results presented by Halstead (1947) of the performance of a larger group of patients do not include mention of their handedness ; but inspection of the table (p. 176) shows that those with left frontal lesions tended to make more errors on " Indicator 2 " (the grouping test) than those with right frontal lesions.

## RESULTS.

The results are presented of the performance of 74 patients with convincingly localized unilateral cerebral lesions on Weigl's Colour-Form Sorting Test. This was administered in the course of a general examination for the presence of organic intellectual impairment ; the pieces were scattered on the table before the patient, who was asked to " sort out the ones that go together " ; to " put the ones together that are the same " ; to " divide them according to some similarity " ; or any phrase that would result in sorting according to one principle (without, of course, mention of the principle involved). When the patient had done this, he was asked to explain in what way the pieces were the same ; if, as often occurred, he was

unable verbally to formulate the principle, it was explained to him; the pieces were jumbled up again; and he was then asked to "sort them another way, not by colour" (or shape, whichever was the first principle used), and so on, until the patient started sorting again. This was the crucial point in the test, upon which we have marked the patients as "passed" or "failed." To pass, the patients had only to sort the pieces correctly according to the remaining principle; in failing, the patients either insisted that they could not see another way of doing it, repeated the previous method of sorting, or began to construct patterns of the pieces, mixing up the similarities.

Table I presents the series of patients, the hospital number, sex, criteria accepted of localization of the lesion and premorbid intellectual level. All the patients were fit enough to walk or come in a wheel-chair to the examiner's room: all were right-handed; and in none was dysphasia, if present, considered sufficiently severe to prevent them understanding the instructions for the test.

TABLE I.

Intelligence is classified according to Wechsler (1944): Superior, Bright Normal, Average, Dull Normal.

| Case No. | Hospital No. | Age. | Sex. | Lesion. | Criteria. | Premorbid intelligence. |
|---|---|---|---|---|---|---|
| *Left Frontal.* | | | | | | |
| 1 | 3520 | 39 | F. | Glioma | Operation; seen | B.N. |
| 2 | 5841 | 35 | M. | ,, | Post-mortem | Av. |
| 3 | 12461 | 36 | F. | Meningioma | Removed | Av. |
| 4 | 13885 | 43 | M. | Glioma | Operation; seen | B.N. |
| 5 | 14712 | 35 | F. | Meningioma | Removed | B.N. |
| 6 | 15613 | 44 | M. | Glioma | Ventriculogram; biopsy | D.N. |
| 7 | 16172 | 56 | M. | ,, | Biopsy | Av. |
| 8 | 16673 | 51 | M. | Vascular accident | Neurological and E.E.G. signs | S. |
| 9 | 23863 | 38 | F. | Glioma | Operation; lobectomy | S. |
| 10 | 24968 | 20 | M. | ,, | ,, ,, | D.N. |
| 11 | 26716 | 34 | M. | Laceration | Operation; seen | B.N. |
| 12 | 3647 | 16 | M. | Gunshot wound | Operation | Av. |
| *Left Fronto-parietal.* | | | | | | |
| 13 | 3842 | 37 | F. | Meningioma | Removed | Av. |
| 14 | 6720 | 37 | M. | Vascular accident | Neurological signs | Av. |
| 15 | 894 | 49 | F. | Glioma | Biopsy | Av. |
| 16 | 13136 | 44 | F. | Meningioma | Removed | B.N. |
| 17 | 16601 | 52 | M. | Vascular accident | Neurological signs | S. |
| 18 | 29219 | 66 | M. | Secondary carcinoma | Post-mortem | Av. |
| *Left Parietal.* | | | | | | |
| 19 | 548 | 23 | F. | Gunshot wound | Operation | Av. |
| 20 | 1874 | 57 | M. | Glioma | Post-mortem | S. |
| 21 | 7812 | 51 | F. | Meningioma | Removed | Av. |
| 22 | 8443 | 45 | M. | Vascular accident | Neurological and E.E.G. signs | B.N. |
| 23 | 9720 | 30 | M. | Ditto | Ditto | Av. |
| 24 | 12055 | 56 | M. | Glioma | Post-mortem | Av. |
| 25 | 13234 | 43 | M. | Meningioma | Removed | D.N. |
| 26 | 19040 | 47 | F. | ,, | ,, | S. |
| 27 | 19103 | 50 | F. | ,, | ,, | Av. |
| 28 | 17956 | 61 | M. | Vascular accident | Neurological signs | B.N. |
| 29 | 17716 | 20 | M. | Glioma | Operation; seen | B.N. |
| 30 | 9411 | 21 | M. | Abscess and atrophy | Operation; ventriculogram | B.N. |
| 31 | 20727 | 43 | M. | Glioma | Arteriogram and E.E.G. | S. |
| 32 | 21590 | 29 | F. | ,, | Biopsy | Av. |
| 33 | 20847 | 65 | M. | Secondary hypernephroma | Post-mortem | B.N. |
| 34 | 22907 | 56 | M. | Angioma | Arteriogram | Av. |
| 35 | 25065 | 22 | M. | Abscess | Operation | B.N. |
| 36 | 29536 | 47 | M. | Glioma | Biopsy | Av. |

TABLE I—*cont.*

| Case No. | Hospital No. | Age. | Sex. | Lesion. | Criteria. | Premorbid intelligence. |
|---|---|---|---|---|---|---|
| *Left Temporal:* | | | | | | |
| 37 | 1794 | 36 | F. | Glioma | Operation; biopsy | Av. |
| 38 | 5522 | 35 | M. | ,, | Biopsy | B.N. |
| 39 | 12926 | 51 | M. | Abscess | Post-mortem | B.N. |
| 40 | 76 | 36 | F. | Calcified cyst | Ventriculogram | Av. |
| 41 | 1680 | 35 | F. | ? Glioma | Arteriogram, A.E.G. and E.E.G. | B.N. |
| 42 | 8375 | 42 | M. | ? ,, | A.E.G., E.E.G. | |
| *Right Frontal:* | | | | | | |
| 43 | 2685 | 21 | M. | Gunshot wound | Neurological and E.E.G. signs | B.N. |
| 44 | 7045 | 54 | M. | Secondary carcinoma | Biopsy | A.N. |
| 45 | 11980 | 43 | M. | Glioma | Lobectomy | S. |
| 46 | 9938 | 44 | F. | Meningioma | Removed | B.N. |
| 47 | 11241 | 31 | M. | Post-traumatic scarring | Lobectomy | S. |
| 48 | 13148 | 41 | M. | Meningioma | Removed | B.N. |
| 49 | 12204 | 43 | M. | Post-traumatic atrophy | A.E.G. | Av. |
| 50 | 15605 | 41 | F. | Meningioma | Removed | B.N. |
| 51 | 11574 | 47 | M. | Glioma | Lobectomy | B.N. |
| 52 | 17310 | 58 | M. | Meningioma | Removed | S. |
| 53 | 20920 | 50 | F. | ,, | ,, | S. |
| 54 | 22601 | 30 | M. | Glioma | Biopsy | B.N. |
| 55 | 22681 | 41 | M. | ,, | Biopsy; decompression | B.N. |
| 56 | 23439 | 56 | F. | ,, | Lobectomy | Av. |
| 57 | 23559 | 27 | M. | Post-traumatic scarring | ,, | ,, |
| 58 | 27179 | 28 | M. | Glioma | ,, | S. |
| 59 | 25687 | 51 | F. | Pituitary tumour | ,, | B.N. |
| *Right Fronto-parietal:* | | | | | | |
| 60 | 484 | 37 | M. | Scarring and atrophy | A.E.G. | Av. |
| 61 | 9140 | 55 | M. | Glioma | Biopsy; A.E.G. | B.N. |
| *Right Parietal:* | | | | | | |
| 62 | 3130 | 55 | F. | Meningioma | Removed | B.N. |
| 63 | 12876 | 46 | M. | Secondary carcinoma | Post-mortem | B.N. |
| 64 | 12592 | 47 | M. | Meningioma | Removed | Av. |
| 65 | 15297 | 53 | M. | Secondary hypernephroma | Ventriculogram | B.N. |
| 66 | 15248 | 52 | F. | Meningioma | Removed | B.N. |
| 67 | 16679 | 47 | M. | ,, | ,, | Av. |
| 68 | 21172 | 47 | M. | Glioma | Biopsy; ventriculogram | S. |
| 69 | 23617 | 63 | M. | ,, | Post-mortem | D.N. |
| *Right Temporal:* | | | | | | |
| 70 | 4586 | 59 | M. | Abscess | Neurological signs | Av. |
| 71 | 8194 | 31 | M. | Glioma | Biopsy; ventriculogram | Av. |
| 72 | 6350 | 60 | F. | ? ,, | Ventriculogram and arteriogram | B.N. |
| 73 | 11315 | 24 | M. | Gunshot wound | A.E.G.; operation | B.N. |
| 74 | 13891 | 36 | M. | Glioma | Post-mortem | S. |

Table II indicates the presence (+) or absence (o) of dysphasia; an estimate of general deterioration based on Wechsler's deterioration quotient and performance on retention tests (1, mild; 2, moderate; 3, marked); and pass (P) or fail (F) on Weigl's test. From these results it will be seen that, while 22 out of 42 patients with left-sided lesions failed the test, only 2 of the 32 right-sided cases did so; and the likelihood that this difference might have arisen by chance in two samples drawn from the same population is less than 1 in 1000 ($\chi_2 = 15{\cdot}6$).

TABLE II.

| Case. | Dysphasia. | Deterioration. | Weigl's test. |
|---|---|---|---|
| *Left Frontal :* | | | |
| 1 | 0 | 3 | F. |
| 2 | 0 | 3 | F. |
| 3 | 0 | 1 | F. |
| 4 | + | 2 | P. |
| 5 | 0 | 1 | F. |
| 6 | 0 | 3 | F. |
| 7 | + | 2 | P. |
| 8 | 0 | 2 | P. |
| 9 | 0 | 0 | P. |
| 10 | 0 | 1 | F. |
| 11 | + | 1 | P. |
| 12 | + | 2 | F. |
| *Left Fronto-parietal :* | | | |
| 13 | 0 | 2 | F. |
| 14 | + | 2 | F. |
| 15 | + | 3 | F. |
| 16 | + | 2 | F. |
| 17 | + | 3 | F. |
| 18 | + | 2 | F. |
| *Left Parietal :* | | | |
| 19 | + | 2 | P. |
| 20 | + | 2 | F. |
| 21 | + | 3 | F. |
| 22 | + | 2 | F. |
| 23 | + | 2 | P. |
| 24 | + | 3 | F. |
| 25 | + | 3 | F. |
| 26 | 0 | 1 | P. |
| 27 | + | 3 | P. |
| 28 | 0 | 1 | P. |
| 29 | 0 | 3 | P. |
| 30 | + | 2 | P. |
| 31 | + | 2 | P. |
| 32 | 0 | 2 | P. |
| 33 | + | 3 | F. |
| 34 | + | 2 | P. |
| 35 | 0 | 2 | P. |
| 36 | + | 3 | F. |
| *Left Temporal :* | | | |
| 37 | 0 | 2 | F. |
| 38 | + | 1 | F. |
| 39 | 0 | 0 | P. |
| 40 | 0 | 0 | P. |
| 41 | + | 2 | P. |
| 42 | + | 1 | P. |
| *Right Frontal :* | | | |
| 43 | 0 | 3 | F. |
| 44 | 0 | 2 | P. |
| 45 | 0 | 1 | P. |
| 46 | 0 | 1 | P. |
| 47 | 0 | 1 | P. |
| 48 | 0 | 2 | P. |
| 49 | 0 | 1 | P. |
| 50 | 0 | 1 | P. |
| 51 | 0 | 1 | P. |
| 52 | 0 | 2 | P. |
| 53 | 0 | 3 | P. |
| 54 | 0 | 3 | P. |
| 55 | 0 | 3 | P. |
| 56 | 0 | 2 | P. |
| 57 | 0 | 2 | P. |
| 58 | 0 | 3 | P. |
| 59 | 0 | 1 | P. |

TABLE II—*cont.*

| Case. | Dysphasia. | Deterioration. | Weigl's test. |
|---|---|---|---|
| *Right Fronto-parietal :* | | | |
| 60 | 0 | 2 | P. |
| 61 | 0 | 1 | P. |
| *Right Parietal :* | | | |
| 62 | 0 | 2 | P. |
| 63 | 0 | 3 | P. |
| 64 | 0 | 3 | P. |
| 65 | 0 | 2 | F. |
| 66 | 0 | 2 | P. |
| 67 | 0 | 3 | P. |
| 68 | 0 | 3 | P. |
| 69 | 0 | 3 | P. |
| *Right Temporal :* | | | |
| 70 | 0 | 2 | P. |
| 71 | 0 | 2 | P. |
| 72 | 0 | 3 | P. |
| 73 | 0 | 0 | P. |
| 74 | 0 | 2 | P. |

This difference remains if the patients with dysphasia are excluded, 8 of 17 left sided, and again 2 of 32 right-sided cases failing ; this difference results in a value for $\chi_2$ of 9·01, which would be significant at the 1 per cent. level with a larger number of cases in one group, but under the circumstances may still be regarded as significant. The same argument may be applied to the difference between left and right frontal cases (7 out of 12 failed ; and 1 out of 17 failed) : $\chi_2$ is 7·24, which would be significant at the 1 per cent. level with more cases in one group, but may nevertheless be considered significant.

Comparing the left-sided cases with dysphasia (14 out of 25 failed) and without (8 out of 17 failed), there is no indication that there is a significant difference between the groups. Comparing the results with different localizations of the lesion in the left hemisphere, the numbers are insufficient for statistical analysis, and the proportions of patients with frontal and parietal lesions are roughly similar ; only with temporal lesions does there seem to be a lower incidence of failure on the test. Inspection of the estimates of general organic intellectual impairment shows that this is not more marked in left-sided than in right-sided cases ;* nor is there a significant difference in the distribution of types of lesion between those on the left and on the right.

## DISCUSSION.

The primary significance of these results lies in their implications for clinical assessment, for they suggest that failure on Weigl's test should be regarded rather as a sign of damage to the dominant hemisphere than as an indication of non-specific dementia. As a test, it is convenient and simple to administer ; unfortunately the problem it presents to the subject is a simple one also, so that, as in the present series, only about 50 per cent. of the cases with dominant hemisphere lesions will be unable to pass it. A more complex sorting test might have greater discriminating value, but, as a preliminary investigation, Weigl's test has the advantage of freedom from elaborate scoring methods and need for standardization.

The theoretical interest of this difference is that it suggests a difference in the part played by each frontal lobe in intellectual functions apart from the more "mechanical" expressive speech function which may be impaired by left frontal lesions. The possibility of a difference has not been suggested previously either by opponents of the view that the frontal lobes play a specific part in intellectual operations (e.g., Kubitschek, 1928 ; Jefferson, 1937 ; Hebb, 1939 and 1941), or by its supporters (e.g., Kolodny, 1929 ; Frazier, 1936 ; Rylander, 1939) ; and it may fairly be inferred that the distinction is apparent only upon presentation of the appropriate problem.

* The evidence of psychometric deterioration with right-sided lesions is explained by the occurrence of memory impairment irrespective of the locus of the lesion (Zangwill, 1943) ; and by frequent impairment on visual-constructive tests with right-sided lesions (McFie, Piercy and Zangwill, 1950).

The differential results do not apply, however, only to the frontal lobes: the distinction holds for lesions elsewhere in the two hemispheres, and suggests that, in the process of abstraction required for completion of the test, the non-dominant hemisphere is little, if at all, concerned. Experience with a verbal test of abstraction (Wechsler's Similarities), which we hope to communicate at a later date, leads to the same conclusion, i.e., that this process is largely the concern of the dominant hemisphere. The present results indicate moreover that the impairment of abstraction shown with left-sided lesions is independent of dysphasia—a conclusion supported by the evidence of more failures and less dysphasia with frontal lesions, but less failures and more dysphasia with parietal lesions (Table II). The findings do not, therefore, support the contention of Goldstein (1948, p. 23) that "the difficulty in finding words—as names for objects—"(the commonest disability in dysphasia: Schiller, 1947) is "the consequence of a change of the total personality, specifically of an impairment of the so-called categorical or abstract attitude";* nor are they consistent with the view that a cerebral lesion results in impairment of abstraction irrespective of its location.

The authors are indebted to members of the Staff of the National Hospital for permission to make reference to their cases and to the results of special investigations carried out in their departments; and to Mr. O. L. Zangwill for his encouragement and advice.

## Summary.

Successful performance of Weigl's Colour-Form Sorting Test involves the ability to abstract from the pieces presented their qualities of shape and colour, and to group the pieces accordingly. In 74 patients with localized cerebral lesions, the incidence of failure on this test is found to be significantly related to the presence of a lesion in the dominant hemisphere, and unrelated to the presence of dysphasia. These results do not support Goldstein's view that a cerebral lesion results in impairment of abstraction irrespective of its location; nor do they support the view that dysphasia is contingent upon impairment of abstraction.

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* It is also noteworthy that not all cases of amnesic (or nominal) dysphasia fail on sorting-tests of the type described in this paper.

# THE USE OF "ETAMON" FOR HIGH BLOOD-PRESSURE IN ELECTROCEREBRAL TREATMENT.

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When electroshock is given, there is generally a rise of blood-pressure for a time. It is therefore stated in various text-books that the treatment is contra-indicated in cases of hypertension. Even premedication with thiopentone and curare does not always succeed in lowering the pressure to a safe level. It is also known that the initial rise in pressure may be followed by a subsequent compensatory fall, so that any drug which prevents fluctuations of arterial tension is likely to be of value. Etamon [tetra-ethyl ammonium chloride (T.E.A.C.)] lowers the blood-pressure by acting on the synapses of the sympathetic nervous system.

Many hospitals have found that electronarcosis is a valuable adjunct to treatment, as it is frequently successful when simple electroshock has failed. On many older patients, however, in whom this treatment is especially useful, the rise of blood-pressure can be very marked; and even forward placement of the electrodes does not always avoid this complication.

At the West London Hospital it was therefore decided to try out the effect of Etamon (Burroughs Wellcome). The bromide salt has the same effect. This drug has been used to lower the blood-pressure in hypertensive states, but there are certain disadvantages in its prolonged use for this purpose. Its administration, however, to combat a temporary rise of blood-pressure lasting 20 to 30 minutes is without any ill effects at all.

We gave the drug, therefore, to a group of 20 cases in order to lower the blood-pressure prior to treatment with electronarcosis. This allowed us to observe the effect of the drug more thoroughly than would be the case with simple electroshock, as the treatment lasted seven minutes.

The following technique was employed in each case:

1. Thorough physical examination including E.C.G.

2. We gave a test dose of T.E.A.C., starting with 2 c.c., intravenously, and injecting slowly up to 3 c.c. No subjective sensation of an unpleasant character was experienced by any patient.

3. The patients were also given, prior to the T.E.A.C., thiopentone 0·2 to 0·5 gm., atropine gr. $\frac{1}{75}$, curare 2 mgm. per stone body weight, or the equivalent dosage of flaxedil. The thiopentone lowers the blood pressure on an average about 27 mm. systolic and 12 mm. diastolic of mercury in these apprehensive, tense patients, and the curare generally has no effect. We had an ampoule of 1·5 c.c. methedrine at hand in case the fall was too marked, but, in fact, it was never used.

The patients were allowed to lie down for 20 minutes before treatment to ensure that physical rest should have its full effect on the blood-pressure.

After the fall of blood-pressure caused by pentothal, the subsequent mean fall due to Etamon for 20 patients was 43 mm. of mercury, systolic, and 32 mm. diastolic.

### Illustrative Cases.

(*a*) Mrs. P—, aged 65. Agitated melancholia with strong suicidal tendencies. Her resting blood-pressure was 220/140 on four occasions.

| | B.P. without T.E.A.C., 7.ii.49. | B.P. with T.E.A.C., 9.ii.49. |
|---|---|---|
| B.P. before treatment, | 220/140 | 150/105 |
| E.N. 1 min., | 230/150 | 127/83 |
| ,, 2 ,, | 230/152 | 170/116 |
| ,, 3 ,, | 225/145 | 165/120 |
| ,, 4 ,, | 220/145 | 160/115 |
| ,, 5 ,, | 230/150 | 150/115 |
| ,, 6 ,, | 235/150 | 150/115 |
| ,, 7 ,, | 230/150 | 155/112 |

Blood-pressure readings were taken after each treatment in this patient for three hours after treatment. The lowest readings were recorded about two hours after treatment. There were no unpleasant symptoms at any time which might be attributed to low blood-pressure.

(*b*) Mrs. J—, aged 53, an obsessional neurosis with depressive features and suicidal tendencies.

| | B.P. without T.E.A.C., 7.ii.49. | B.P. with T.E.A.C., 9.ii.49. |
|---|---|---|
| B.P. before treatment, | 233/142 | 103/100 |
| E.N. 1 min., | 241/120 | 185/137 |
| ,, 2 ,, | 241/146 | 190/119 |
| ,, 3 ,, | 236/138 | 187/119 |
| ,, 4 ,, | 233/140 | 212/127 |
| ,, 5 ,, | 233/140 | 194/124 |
| ,, 6 ,, | 235/135 | 216/120 |
| ,, 7 ,, | 233/127 | 205/120 |

In this case, also, the lowest readings were recorded two hours after treatment.

Both these patients made a complete recovery from their severe depressions, one being with obsessional symptoms. But for T.E.A.C., however, treatment would have been hazardous or contra-indicated.

(*c*) Mr. B—, aged 49, an agitated depression with a reactive factor in his recent history—he made an attempt at suicide by hanging himself with a rope a week before treatment.

| | B.P. without T.E.A.C., 12.ii.49. | B.P. with T.E.A.C., 15.ii.49. |
|---|---|---|
| B.P. before treatment, | 260/107 | 135/82 |
| E.N. 1 min., | 230/147 | 140/102 |
| ,, 2 ,, | 197/130 | 150/117 |
| ,, 3 ,, | 192/135 | 152/117 |
| ,, 4 ,, | 190/132 | 160/120 |
| ,, 5 ,, | 190/137 | 165/117 |
| ,, 6 ,, | 200/137 | 172/122 |
| ,, 7 ,, | 202/137 | — |

(*d*) Mrs. K—, aged 29, a catatonic schizophrenic, who had been twice in mental hospitals for suicidal attempts, and who came to us a week after discharge from an observation ward, following a suicidal attempt with 40 gr. of Seconal. She had a total of 60 electro-narcoses and has remained well for three years, doing a difficult job as a designer.

| | B.P. without T.E.A.C., 12.iii.48. | B.P. with T.E.A.C., 14.iii.48. |
|---|---|---|
| B.P. before treatment, | 160/110 | 125/100 |
| E.N. 1 min., | 180/124 | 135/105 |
| ,, 2 ,, | 182/127 | 155/100 |
| ,, 3 ,, | 188/128 | 155/100 |
| ,, 4 ,, | 180/122 | 147/105 |
| ,, 5 ,, | 185/127 | 124/86 |
| ,, 6 ,, | 185/120 | 120/80 |
| ,, 7 ,, | 180/125 | 140/96 |

(*e*) Mr. A—, aged 72, a recurrent endogenous depression who was suicidally depressed.

| | B.P. without T.E.A.C., 17.v.49. | B.P. with T.E.A.C., 21.v.49. |
|---|---|---|
| B.P. before treatment, | 200/130 | 160/105 |
| E.N. 1 min., | 210/140 | 175/120 |
| ,, 2 ,, | 260/150 | 200/110 |
| ,, 3 ,, | 270/160 | 180/110 |
| ,, 4 ,, | 202/127 | 170/115 |
| ,, 5 ,, | 210/130 | 160/100 |
| ,, 6 ,, | 198/129 | 155/95 |
| ,, 7 ,, | 192/133 | 150/93 |

## Summary.

1. All the twenty cases responded in like manner with a good average drop of blood-pressure, which did not rise to dangerous heights during treatment, as it had done previous to T.E.A.C.

2. We observed no untoward effects clinically, and the patients did not complain subjectively of any unpleasant effects after the treatment. Seven said that they did not have a severe headache after treatment, of which they had complained when no T.E.A.C. was administered.

3. Where, in addition to hypertension, two cases had anginal symptoms on effort, we gave the patients twice their usual dose of glyceryl trinitrite prior to treatment.

We should like to express our thanks to Dr. H. Crichton-Miller, Medical Director of Bowden House, for access to two of his patients; to Dr. F. Prescott of the Wellcome Research Institution for providing us with the Etamon; and also to the Dan Mason Research Fund, under whose auspices this work was done.

# SCHIZOPHRENIA: A NEW APPROACH.

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## Introduction.

Mr. Gladstone, with that candour which a great Statesman can afford, once said, "Government is a rough business, and the results are most unsatisfactory." Unfortunately no great psychiatrist has described the present state of our knowledge and treatment of schizophrenia in an equally robust phrase; but surely, "rough business and unsatisfactory results" would not be an unfair summing up?

We have now known of this illness for nearly half a century, and yet our understanding of it is slight and our useful information scanty. This is not because we have been idle, but because our efforts have been poorly rewarded. Thousands of papers are written every decade; tens of thousands of observations are made; there is no lack of opportunity for studying patients when about one hospital bed in five in this country is occupied by a schizophrenic, yet we are still entirely ignorant of the cause of this disease. There are, it is true, numerous theories, but none is generally accepted. We have one form of treatment, deep insulin, which produces remission of symptoms in some cases and what seems to be a cure in others, but even the value of this treatment is hotly disputed. Because deep insulin is a purely empirical procedure the psychiatrist is always tempted to become preoccupied with details of technique so that he forgets, or at least becomes less aware of our fundamental ignorance.

## The Present Situation.

Since Bleuler (1), over forty years ago, defined schizophrenia in his great monograph, and advanced the hypothesis that it was a metabolic disorder with manifestations in the psyche, the bodily functions of schizophrenics have been studied intensively, but these investigations have not, with few exceptions, been illuminating, and where some abnormality has been found this can usually be accounted for by the poor condition of the patients. This is no place to catalogue the extraordinary efforts of nearly two generations of research workers, but an observer is astonished by the ill-rewarded zeal and activity. No stone has been left unturned; indeed showers of stones seem to have been thrown up indiscriminately. From Bellak's (2) extensive survey it is clear that not everyone agrees with Bleuler that schizophrenia is a metabolic disorder. The psychoanalysts hold with more or less tenacity that the illness is largely psychogenic. In their view, so far as an uninitiated person can summarize it, the schizophrenic, unable to adjust to difficulties occurring in very early childhood, retires into a fantasy world when confronted with some insupportable situation later in life. Between these polar opposites there is plenty of scope for theorizing, and there has been no lack of it. Nutritional disorders, head injury, infections including syphilis and tuberculosis, hereditary and various endocrine deficiencies have all been implicated, and either in concert or separately have their supporters.

## Treatments.

Where causation is obscure, treatment is usually varied. In this illness it extends from the highly intensive and often non-verbal psychotherapy used by Rosen, through more formal psychoanalysis, to a whole range of physical therapies including electrical and insulin shock, freezing and over-heating, increased oxygen intake and nitrogen inhalations. Psychosurgery is also used, and at the other end

of the scale are those who believe in custodial care and eugenic advice. Insulin shock alone has received some measure of general approval, but even here there is no agreement as to how it works, and some disagreement about whether it works.

### The Future.

Future campaigns planned include sociological studies, special psychoanalytic techniques, refined shock therapies, more accurate surgery, and fuller endocrinological and biochemical investigations. Gjessing's (3) scheme is an example of the type of prolonged study from every angle which it is hoped will solve the problem. He suggests that a group of schizophrenics should be studied in every conceivable way for an indefinite period; at the end of some long time he believes something valuable will emerge: but are these hopes justified? The body is prodigal in its chemical syntheses, and an experiment of this sort might go on indefinitely, bringing nothing but discouragement. The toxic substance, if toxic substance there is, may not be easily identifiable because its effects may be largely psychic and there may be only slight physical disturbances in animals. It is difficult to be sure when a guinea-pig is deluded. A substance whose most important properties were only discoverable by human experiment would remain long hidden until someone happened to know what he was looking for, which no one at present does.

### A New Approach.

It is possible, however, to approach the illness from another direction. Suppose that we start with the signs and symptoms and natural history of schizophrenia and ask ourselves how these could be produced, refusing to be diverted by the existing schools of thought.

There are no constant physical findings, but Hoskins (4), who has had a unique opportunity to study the illness, agrees with many others that disorder of the adreno-sympathetic system is one of the most constant features. Mott (5) some years ago observed some peculiarity in the adrenal medulla in schizophrenics, but he became more interested in the gonads and the matter seems to have been dropped. Early in the illness physical symptoms of anxiety are often found, but these die out as the illness progresses. It is as well to emphasize that the majority of authorities are agreed that there is no physical pathology known in schizophrenia.

The psychic symptoms are disturbances of association, thought, mood, and behaviour without dementia. Delusions and hallucinations occur frequently, and disturbances of bodily function lumped together as catatonia are important. The illness may sweep down in a few hours or may be very insidious. It may last a few days or a whole lifetime. Acute onset is usually considered a good prognostic sign, but it is not a certain one. An early response to treatment is also looked on as a good augury, but people who have been degraded lunatics for years have been known to recover long after treatment has failed. Now that schizophrenics are surviving longer than in the past, more cases are being seen in which the illness has died out in late middle age, leaving behind a socially crippled person who is not, however, a schizophrenic.

There is evidence that shy, shut-in people are more liable to schizophrenia than outgoing folk, but this is disputed, and some psychiatrists maintain that the "shut-inness" is just an early stage of the illness. What is certain is that people who apparently enjoyed excellent physical and mental health have been struck down by it. Most doctors agree that long thin people are more likely to develop it than short fat people.

No age is exempt, but the first attack usually occurs in young adulthood. Psychological investigation has yielded little except that clever and stupid people are equally affected.

Its association with difficulties in early life is uncertain and by no means proved; it is often hard to decide when the illness began, because the childhood disturbances may only be early symptoms. Psychoanalytic evidence is vitiated by the lack of an objective standard due to the paucity of published analyses of normal people. We have therefore no sure means of telling whether the schizophrenic usually has a more unhappy childhood than the non-schizophrenic, but it is certainly not unknown for schizophrenics to have histories which suggest a happy and contented childhood.

We must therefore account for a situation in which a person of any age, but usually a young adult, in response to stress or with little evidence of it, becomes

slowly and insidiously, or with overwhelming speed and accompanied by acute confusion, subjected to disturbances of association, changes in affect, thought disorder, hallucinations and delusions and catatonic symptoms to such an extent that life outside a mental hospital becomes impossible. The sick person, on the other hand, may never even need to visit a doctor but may simply appear odd and eccentric. The illness may terminate quickly either with or without medical aid, or may be completely resistant to any form of treatment and continue for years without any pathognomonic physical changes being demonstrable. It must be influenced by a wide variety of treatments, such as psychoanalysis, deep insulin, metrazol, E.C.T., thyroid therapy and leucotomy. Occasionally events such as a severe physical illness or a psychic or physical shock may affect it favourably. It must be possible for the patient to recover after years of illness without measurable evidence of intellectual impairment, and to appear remarkably normal in spite of a long period of incarceration. The illness should bear some understandable relationship to the manic-depressive disorders, and not infrequently be indistinguishable from them at an early stage. It would be in keeping with our present knowledge if an inherited constitutional basis could be provided for its occurrence.

## The Synthetic Illness.

The first question that one asks is whether any known substance could produce results of this sort ; not merely confusion with secondary delusions, but a disturbed mental state which could be mistaken for schizophrenia. It has been known for over fifty years that mescaline, the alkaloid extracted from the peyotl—*Anhelonium Lewinii*, an American cactus—produces symptoms almost identical with schizophrenia, including catatonia and thought disorder. The symptoms differ in different subjects, but not more markedly than different cases of schizophrenia differ. No account of the effect of altering the dosage of mescaline in the same subject has come to our notice, so that it is impossible to decide whether the difference in symptoms is due to differences in rates of absorption, or the ratio of body weight to dose, or to other factors. It has been taken for years by psychiatrists who wish to experience schizophrenic symptoms and to investigate synaesthesia. From time to time investigators have mentioned that it is unfortunate that more is not known about it. Klüver (6) in America and Eric Guttmann (7) in this country drew attention to our ignorance on this subject and to its importance respectively ; but are we really so ignorant ? The formula of mescaline has been known for at least twenty-five years, and probably much longer. It had not, however, been published in a psychiatric paper for many years until Mayer-Gross's recent lecture (8). Unfortunately in this paper the formula was misprinted, and in addition the structural diagram was so arranged that its most remarkable quality was obscured. Organic chemists have, of course, known its biochemical affinities for many years, but they have rarely been interested in its psychological properties.

There are many other hallucinogenic drugs, but none has either such striking properties or such a simple chemical constitution as mescaline. It would therefore be an excellent candidate for a schizophrenic agent, if there were any likelihood of its appearing in the body.

Before discussing this question it is necessary to examine a widely held view whose most recent proponent is Mayer-Gross. To quote his own words : " The symptoms of mescaline intoxication have been compared to those of schizophrenia, but it is much more the strangeness experienced by the patient suffering from schizophrenia and the difficulties of describing what is happening in the two conditions which is similar. Many typical schizophrenic symptoms, especially in subacute and chronic states, are never seen in mescaline intoxication. Early psychotic phenomena in acute schizophrenia show certain analogues, especially in the field of hallucinations and other sense abnormalities " (8). Surely, in trying to lump together acute and chronic schizophrenic reactions and compare them with the laboratory observations of trained psychiatrists taking mescaline voluntarily, Mayer-Gross is comparing two innately different situations. It is highly unlikely that the unheralded schizophrenic psychosis of indefinite duration in an unprepared victim, and the experiences of a voluntary mescal taker who knows what to expect and how long his ordeal will last, would be exactly similar. The remarkable thing is that these acute reactions have so much in common. In the accompanying table it will be seen that mescaline reproduces every single major symptom of acute schizophrenia, although not always to the same degree.

TABLE I.—*A Comparison between the Psychological Effects of Mescaline and the Symptoms of Acute Schizophrenia.*

| | Mescalin. | | Acute schizophrenia. | |
|---|---|---|---|---|
| | Illusions. | Hallucinations. | Illusions. | Hallucinations. |
| 1. *Sensory disorders:* | | | | |
| *a.* Vision | xxx | xx | xx | xx |
| *b.* Hearing | x | x | xx | xx |
| *c.* Body image | xxx | — | xx | — |
| *d.* Smell and taste | xxx | xxx | xx | xx |
| *e.* Skin sense | xx | — | xx | — |
| *f.* Temperature | xx | — | xx | — |
| *g.* Synaesthesia | xxx | — | ? | — |
| 2. *Motor disorders:* | | | | |
| *a.* Catatonia | xx | | xxx | |
| 3. *Behaviour disorder:* | | | | |
| *a.* Negativism | xx | | xxx | |
| *b.* Withdrawal | xx (big doses) | | xxx | |
| *c.* Antisocial violence | Reported | | xx | |
| 4. *Thought disorder:* | | | | |
| *a.* Pressure | xx | | xx | |
| *b.* Disturbed association | xxx | | xxx | |
| *c.* Blocking | xx | | xxx | |
| *d.* Substitution of *primitive thinking* in the form of visual images for conceptual thought | xxx | | xxx | |
| *e.* Neologisms | x | | xx | |
| 5. *Disorders of interpretation:* | | | | |
| *a.* Ideas of influence | xx | | xxx | |
| *b.* Paranoid ideas | xxx | | xxx | |
| *c.* Heightened significance of objects | xxx | | xx | |
| 6. *Delusions* | xx (time factor) | | xxx | |
| 7. *Splitting* | xx (time factor) | | xxx | |
| 8. *Depersonalization* (*a*) | xx | | xx | |
| Derealization (*b*) | xxx | | xxx | |
| 9. *Mood disorders:* | | | | |
| *a.* Fear and terror | xxx | | xxx | |
| *b.* Depression | x | | x | |
| *c.* Indifference and apathy | xx (time factor) | | xxx | |
| *d.* Manic symptoms | x | | x | |
| *e.* Euphoria | xxx | | xx | |
| *f.* Schizoid humour | xx | | xx | |
| 10. *Insight* | Sometimes absent (time factor) | | Sometimes present | |

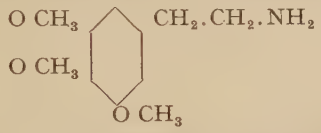
o, does not occur. x, occurs. xx, marked when it occurs but not always present. xxx, marked and frequent. —, not relevant.

We have actually noted in our six subjects all these effects of mescaline except 1(*b*) reported by Rouhier (15) and Tayleur-Stockings (16) and 3 (*c*) reported by Hey (17).

Subacute and chronic schizophrenia cannot be compared legitimately with acute mescaline poisoning, but should be compared with chronic mescaline intoxication. Very little seems to be known about this condition, and one of the few references to it known is quoted in Mayer-Gross's lecture. It reads : " The use of the drug was, and probably still is, a problem to the Christian Missionaries who insist that its regular intake leads to increasing laziness and impairment of will-power." Surely a lay person might describe a chronic schizophrenic in such a phrase ? May it not be that to use his own words, " the strangeness experienced by the patient suffering from schizophrenia and the difficulties of describing what is happening in the two conditions " constitute an essential similarity ? Language is not designed to depict the weird world of the mescaline taker and the schizophrenic. Only very rarely is the latter willing or able to describe his experiences coherently. When he does, as in Henning's (9) astonishing book *The Witnesses*, the world which he describes is more like that of the mescaline taker than any other.

The objection that all the symptoms of schizophrenia are not found in acute mescaline poisoning is not valid. So far as one can judge from the little evidence available, the effects of mescaline vary as much as but not more than the symptoms of schizophrenia, which unhappily for psychia'rists allows a wide range of variability.

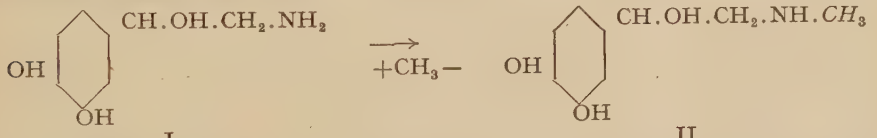
To return to the chemical constitution of mescaline, which is—




it is a fairly simple compound, and those with biochemical knowledge will realize that it is not very dissimilar from adrenaline. This observation was made by one of us in June, 1950, with the assistance of Dr. Julian Redmill, then a medical student at St. George's Hospital. The adrenergic qualities of mescaline and many similar drugs were investigated by Dr. J. Harley-Mason, M.A., F.R.I.C., University Demonstrator in Organic Chemistry at Cambridge. He has been good enough to allow the following biochemical observations on this aspect of the subject to be published.

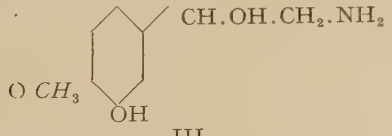
### Biochemical Note.

He writes : " It is extremely probable that the final stage in the biogenesis of adrenaline (II) is a transmethylation of nor-adrenaline (I), the methyl group arising from methionine or choline.

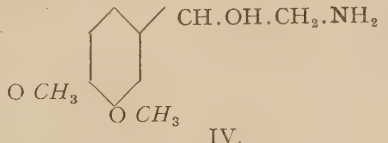



I. II.

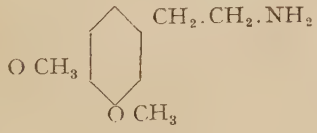
It is just possible that a pathological disordering of its transmethylation mechanism might lead to methylation of one or both of its phenolic hydroxyl groups instead of its amino group, leading to the formation of (III) and (IV). Methylation of phenolic hydroxyl groups in the animal body is of rare occurrence, but a significant case has been reported recently by Maclagon and Wilkinson (10). It is particularly interesting to note that out of a series of phenylethylamine derivatives tested by Noteboom (11), 3.4-dimethoxyphenylethylamine (V) was the most potent in producing catatonia in animals, and that this substance




III.




IV.




V.

differs from (IV) only in the absence of its side chain hydroxyl group. It is however doubtful, in view of the relatively high dosage of (V) required to produce a catatonic effect, whether enough of a compound such as (IV) could be elaborated in the body to produce mental symptoms, having regard to the normal capacity for adrenalin production. It may be, however, that in chronic intoxication smaller amounts would be effective.

"The extremely high activity of lysergic acid diethylamide is remarkable, the dosage level of 30–50 mgm. being one-tenth the amount of adrenalin or thyroxin required to produce an observable response. The compound bears no relationship to any substance at present known to occur in the animal body and the mechanism of its action is wholly obscure."

Surely it is significant that a single biochemical failure could occur in the stress mechanism and produce these dangerous toxins, one of which is already known to be a powerful catatonic agent? Mescaline itself is not, of course, the toxic agent in schizophrenia. It is not nearly active enough, and the adrenals could not possibly make 500 mgm. or more daily, which would be necessary to produce symptoms. It is, however, thought that mescaline itself is non-toxic, and that the toxic agent in mescalism is a breakdown product.

We therefore suggest that schizophrenia is due to a specific disorder of the adrenals in which a failure of metabolism occurs and a mescaline-like compound or compounds are produced, which for convenience we shall refer to as "M substance." The striking implications of the relationship between the bizarre Mexican cactus drug and the common hormone have, so far as we know, never been recorded before. Psychiatrists appear to have been unaware of its biochemical structure, biochemists to have been uninterested in its production of an artificial psychosis. The close clinical connections between schizophrenia, anxiety states and stress have been known for a long time, and the process involved may be that in certain people when the adrenals are overworked (due perhaps to an inherited latent fault as Kallman has suggested) (12) the process of methylation becomes disturbed and highly toxic substances are produced. This M substance, once produced, would naturally set up a vicious circle, since one of the prominent features of both the mescal "psychosis" and of many cases of schizophrenia is the stress and terror experienced by the victim. There is already a certain amount of evidence for the presence of such an agent (13). This hypothesis could also account for the somatic manifestations of schizophrenia—the excessive adrenocortical activity perhaps generated by Vogt's mechanism, the vascular changes, the disturbances of carbohydrate metabolism, the overloading of the detoxicating mechanisms of the liver, and the pigmentation (melanin and adrenaline metabolism are linked).

The result of these endogenous disturbances in sensation, feeling and thought upon the sick person would depend on the age of onset, the rate at which M-substance is produced, the patient's previous personality and special mode of reaction to M-substance, and the cultural setting in which the illness occurs. These variables allow for the enormous range of different reactions such as is actually observed in schizophrenia, which could thus appear to have many and various "precipitating causes."

Similarly, many forms of treatment could be expected to alleviate the condition to some extent—acute physical illnesses with their general metabolic upset: psychotherapy, where the attempt made to help the patient adapt to his strange new environment might serve to break the vicious circle by alleviating the stress experienced and thus depressing the production of M-substance; leucotomy, which might break the circle at the level of cerebral reaction to stress; and lastly and most significantly the only generally accepted treatment, insulin, is itself an anti-adrenaline agent. Further, since it is known that mescaline produces its effects by interfering with the glucose metabolism of the brain, the beneficial effects of insulin treatment may be produced, not so much by the comas, as by the large amount of glucose that is forced into the bodily metabolism. It is of interest that Mayer-Gross (14) reports that high doses of glucose raising the blood sugar above 200 mgm. inhibit the action of lysergic acid (LSD. 25).

Many of the results of schizophrenia have little to do directly with disturbances of brain function, but depend on factors which are, in the anthropological sense, cultural. The isolation and dislike which the patient experiences in our community forces him to retreat into his private world. The schizophrenic regresses because, faced with an incomprehensible change in his external and internal sur-

roundings, his painfully learned patterns of behaviour suddenly become useless and he is left isolated and enmeshed in his own fantasies and the phantasmagoria produced by M-substance. He is literally and not figuratively out of touch with his environment. In societies different from our own the results of this universal metabolic abnormality (the production of M-substance) may be socially beneficial to the individual. For instance the Shamans in Siberia and the Mystics in Tibet are in fact leaders of society though undoubtedly having schizophrenic experiences.

## Discussion.

It is easy enough to speculate about an illness which has been the subject of so much investigation and remains so barren in established aetiology, but the first essential for any directed programme of research is a hypothesis based on fact, otherwise observation hardly progresses beyond the stage of cataloguing. It seems to us that the advantage of this new approach lies in its combination of the clinical and the biochemical, which allows one to substitute a definite plan of campaign in place of the present state of speculation about unknown substances. Mescaline is the simplest agent producing a schizophrenic-like psychosis, and the only one that closely resembles a substance found naturally in the body. The proper course of action to test this hypothesis is clear. It would consist in the pharmacological investigation of mescaline, its breakdown products, and the range of compounds between it and adrenaline (especially 3.4-dimethoxyphenylethylamine), and the attempt would have to be made to isolate these substances from the body-fluids of acute schizophrenics. Once these investigations have been done our hypothesis will either join the large number of plausible theories which have failed to stand up to the test of experiment and are now to be found on the scrap-heap of psychiatry in the pages of old journals, or the cause of schizophrenia will be known.

## Summary.

After a brief survey of the present state of our knowledge regarding schizophrenia we have drawn attention to the close biochemical relationship between adrenaline and mescaline. This, taken in conjunction with the clinical relationship between acute mescaline intoxication and acute schizophrenia, and between the latter condition and stress, appears to us to be significant. The clinical and biochemical implications of this are discussed.

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# A COMPARATIVE STUDY OF THE CAUSATION OF MONGOLISM, PERISTATIC AMENTIA, AND OTHER TYPES OF MENTAL DEFECT.

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MENTAL deficiency has been defined by Tredgold as a state of arrested or incomplete development of the mind. Numerous scientists have for long endeavoured to ascertain the cause or causes of this frequent abnormality. The protagonists of one school of thought made exaggerated claims that the great majority, if not all cases, were due to hereditary factors. Other investigators were able to demonstrate that certain special types of mental defectives owed their deficiency to agents acting after fertilization, and so came to the conclusion that genetic elements were only concomitant and not primary causative factors in many, if not in all types of defectives, and that research on these lines should eventually establish extrinsic causation in all these cases.

Thus one has gradually come to distinguish between two main groups of mentally abnormal individuals ; those in whom endogenous or hereditary factors could be proved or at least suspected. (Tredgold speaks of primary aments, Strauss of endogenous types, and those in whom exogenous noxious influences could be demonstrated or suspected, and whom Tredgold termed secondary aments, Strauss calls exogenous types.) According to Tredgold and many other investigators, from between 70 to 80 per cent. of all defectives are to be found in the first group, while roughly 20 to 30 per cent. belong to the second. Penrose's figures in support of a hereditary causation are even higher.

A number of mentally deficient persons will always be encountered in whom both hereditary and environmental factors will be present. Yet, one of the two will be predominant to such an extent as to enable us to include the case in question in the first or second group of aments, and to consider the less predominant factor as concomitant only. Eventually, we shall come across cases where we shall not be able to establish proof of either a genetic or an environmental causation. These are the case where factors must be or must have been active of whose presence, mode of action and time of damaging influence we have yet to gain knowledge. Science has advanced very considerably in this field lately, and we owe a great deal especially to Professor Penrose for his research on genetic lines.

This paper is intended to show that there exists a distinct difference in aetiology between Mongolism on the one hand, and all the other types of mental defect on the other. The paper is based on a careful study of 555 ordinary defectives of all grades and types and of 150 Mongols. A larger number of both groups was primarily selected for investigation, but in the course of examining every single case the reliability of informants and data in many cases became rather doubtful, and numbers of them had to be excluded. The procedure was to send a questionnaire to the mothers of the defectives—and to mothers only. It was, however, found that many were not answered at all, others incompletely and unsatisfactorily. Thus I was compelled to abandon this method of investigation and to interview the mothers in question personally instead. I am naturally aware that the validity of statistics depends to a considerable extent on skilful interrogation, on the establishment of trust and confidence between the informant and the investigator and, in the first place, on the reliability of the interviewed person. As far as one is able to do so, the data relating to the 705 cases have been checked very carefully and are considered to be reliable.

Of the 555 defectives of all types with the exception of Mongols, 99 or 17·85 per cent. were feeble-minded, 414 or 74·57 per cent. imbeciles of all grades, and 42 or 7·58 per cent idiots. Among them were represented :

158 epileptics = 28·45 per cent.
47 who had a superimposed psychosis either of the schizophrenic or of the paranoid type = 8·46 per cent.
26 suffered from spastic pareses of various degrees,
16 from congenital hemiplegia,
12 from choreo-athetosis,
14 from congenital deaf-mutism.

Other conditions include congenital syphilis (3 cases), muscular dystrophy (3 cases), syringomyelia (1 case), microcephaly (2 cases), hydrocephaly (2 cases), achondroplasia (1 case), juvenile G.P.I. (1 case), post-encephalitic Parkinsonism (1 case), paralysis due to poliomyelitis (1 case), congenital blindness (2 cases), hypertelorism (1 case), and sensory aphasia (1 case).

It can clearly be seen that a great variety of defective is presented in this sample of 555 cases. As to the aetiology of their deficiency, in 201 cases (36·2 per cent.) there was ample evidence to justify the assumption of a genetic causation. Many patients were the offspring of parents one or both of whom were defectives themselves. In many instances the parents or one of them are now inmates of asylums. In others, nearest relatives, such as brothers and sisters or grandparents are or were afflicted. According to many leading scientists in this field, not only mental deficiency among nearest relatives is claimed as a criterion for their hereditary theories, but also other mental illnesses, such as schizophrenia, psychoneurosis, epilepsy and others. While this view is strongly supported by many, it is just as strongly opposed by Kallmann, Barrera, Hoch and Kelley, who studied the frequency of mental deficiency in the blood relatives of schizophrenics. They do not accept explanations based entirely on lower animal and plant experimentations, explanations that, as Sarason points out, are given weight " because there are no other testable assumptions which can explain the available facts or make as accurate predictions."

In quite a number of these relatives there were various congenital malformations either of an identical nature to that found in their defective offspring, or of a quite different type. It will be remembered that among many others, Charles Hermann in America, Péhu and his co-workers in France and Tobler in Germany attributed great importance to the presence of malformations in the families of mentally defective individuals, and concluded that genetic factors were responsible for both the mental and the physical anomaly. Doxiades and Portius also subscribed to this view. On the other hand, there is now ample evidence available to show that genetic as well as environmental factors may lead to malformations of the same type. This means that one and the same malformation may be caused by hereditary factors in one case, by environmental in another. Warkany, for example, points out that congenital cataract may be genetically determined and inherited as a dominant characteristic in one case, but may be due to maternal rubella and thus not be hereditary in another, or that microcephaly may be caused genetically in one case, by maternal rubella or by toxoplasmosis or by irradiation of the lower abdominal and pelvic regions in others.

In addition to these 201 cases, there were another 165 cases (29·7 per cent.) in whom hereditary factors were present in addition to environmental agents, yet so predominant that a genetic causation could easily be assumed. The total figure of roughly 66 per cent. is slightly below the average in the literature.

The mode of transition is still strongly disputed. Some students still believe in the transmission of a defective type of germ plasm from generation to generation without any alteration in the course of this transmission. This view, originally held by Davenport, is not greatly favoured by Tredgold and others.

A specific germ abnormality is sponsored to lead to special rare types of mental deficiency. To name only a few : Tuberous sclerosis has been shown by Gunther and Penrose to be due to a single dominant gene, this also applies to Huntington's chorea and to brachydactyly, while phenylpyruvic oligophrenia and amaurotic family idiocy are supposed to be caused by recessive genes. Among others, Jervis found 213 cases of phenylpyruvic oligophrenia in a sample of 20,300 patients, and strongly supported the idea of a recessive gene. In the great majority of other

types of deficiency it is, however, suggested that the responsibility lies not in one single gene, but in a combination of several dominant or several recessive or even in a combination of dominant and recessive genes.

Recently much evidence has been collected to show that these two modes of transmission are only rarely encountered, and then only in certain specific types of aments, and that a corruption or impairment of the germ cells takes place which is, eventually, responsible for the deficiency. Environmental factors, such as heat X-ray irradiations of the lower abdominal region, poisons such as quinine, arsenic, mercury and others, the toxins of syphilis and tuberculosis, and, according to some investigators, long-standing indulgence in alcohol, are thought to lead in some cases not quite to a destruction of the germ cells and eventually to abortion, but to serious impairment of them, resulting in deficiency.

There is some experimental evidence in animals and plants for the above views. Evidence in man, however, is still wanting. That certain types of defectives conform strictly to Mendelian laws can now be taken for granted, but in the very great majority of cases we are still unable to prove how many genes are implicated, what their combination is, what significance sex linkage has, and so on. It is not the purpose of this paper to discuss genetics in detail. My object was to point out the still immense complexity of the problem in spite of enormous progress in recent years.

Let us now consider environmental factors among my cases. We have learned that the placental circulation is responsible for the nutritional supply to the embryo. Any noxious factor interfering adversely with this placental circulation must necessarily bring about inadequate nutrition of the embryo and cause a variety of malformations, in the first place damage to the brain resulting in mental deficiency. These factors can be active shortly before conception, as has been reported in some cases of maternal rubella. They can act shortly after conception and, eventually, throughout all the stages of the pregnancy up to the time of delivery. Many are the factors that have been cited in the literature in this connection, from direct damage to the uterine mucosa through curettage to infections and intoxications of various types, penetrating the chorionic barrier and so producing severe lesions in the embryo. To mention only a few: S. Lamm and F. Schreiber have shown that in a number of instances prolonged loss of oxygen during the various stages of pregnancy resulted either in mental or physical impairment of the child. In some cases, however, no obvious damage was caused in spite of prolonged anoxia. As Reese and Ingalls have stated, placental haemorrhages are mostly responsible for this foetal anoxia. Murphy, Shirlock and Doll reported that 51 per cent. of the offspring of 53 mothers receiving X-ray treatment during pregnancy were abnormal in one way or another, 26 per cent. being microcephalic. Stewart has suggested that some cases of cerebral palsy may be due to lack of vitamins. He has examined the brains of 50 diplegics and found structural changes very similar to those found in avitaminosis. Since the publications of Gregg, followed by those of Swan, Evans, Carruthers, Reese, Simpson, Martin, Parsons and many others, we know of the serious damage caused by maternal rubella in the early stages of pregnancy. Shortage of time and space do not allow me to enumerate in detail so many more exogenous factors mentioned in the literature.

Among my 555 cases a miscarriage had preceded the birth of the defective in 24 instances, = 4·32 per cent. Of these, seven cases, = 1·26 per cent., had been curetted; in the remainder either falls, shock or old age were blamed for the abortion, while in a few cases no cause whatever could be elicited in the interview. The interval between the miscarriage and the following pregancy ranged from six weeks to six months in 19 of these cases. In the remaining five the interval was longer; however, in these latter cases the age of the mothers was rather advanced. In addition to these, there were nine mothers in who, either a severe haemorrhage had occurred in the course of the pregnancy, or a uterus or a vaginal prolapse operation had preceded the pregnancy, which terminated with the birth of the defective child. In another nine cases mothers had tried to procure abortion by the intake of abortifacients, or by administration of lysol or other irritant irrigations to the vagina. These attempts had not been successful enough to end with an abortion, but may have been instrumental to cause serious damage to the nutritional supply in the uterine mucosa. If we add these 18 cases to the aforementioned 24, we have a total of 42 cases, or 7·56 per cent., in whom a pathological condition of the uterine mucosa may have been the causative agent. That this figure con-

trasts enormously with the corresponding figure in Mongolism will soon be apparent.

In this connection may be mentioned B. Landtmann, who made a comparative study at University College Hospital of the relationship between the maternal condition in pregnancy and congenital malformations of the foetus. He stated that 19·5 per cent. of the mothers of malformed children had had previous abortions, compared with 7·5 per cent. in the control group. In 20·5 per cent. of the mothers of malformed children there had been ante-partum haemorrhages, in the control group only in 4·5 per cent.

In many text-books and papers dealing with mental deficiency it is pointed out that the first-born, especially in a very young mother, is sometimes a defective, while the following pregnancies terminate with the birth of normal children. In addition, old age of the mothers, large series of pregnancies and a large interval between the preceding pregnancy and that leading to the birth of the defective child are also blamed for the deficiency.

The following table shows that :

37 children, 6·7 per cent., were born of mothers before the latter had reached the age of twenty years,
425 children, 76·6 per cent., between the ages of 20 and 35 years, and
93 children, 16·7 per cent., between the ages of 36 and 50 years.

Thus, of the 555 children, 462, or roughly 83·3 per cent., were born before the mother had reached the age of 35 years, in other words, during the best child-bearing period. We shall see how greatly this contrasts with our findings in mothers of Mongol children. If we admit the possibility or probability of the uterine mucosa not being at its best before the age of twenty years, these figures must be adjusted to only 425 children, or 76·6 per cent., being born during the optimal period of woman's fecundity.

After the age of forty years only 23 children or just over 4 per cent. were born.

*Table showing the Ages of the Mothers at the Time of the Birth of the Defective.*

| Ordinary defectives of all grades. | | Age of the mother. | Mongols. | |
|---|---|---|---|---|
| Number of children. | Per cent. | | Per cent. | Number of children. |
| 37 | 6·7 | Below 20 | 2·7 | 4 |
| 172 | 31·0 | Between 20–25 | 2·0 | 3 |
| 155 | 28·0 | ,, 26–30 | 7·3 | 11 |
| 98 | 17·6 | ,, 31–35 | 18·0 | 27 |
| 70 | 12·6 | ,, 36–40 | 31·4 | 47 |
| 19 | 3·4 | ,, 41–45 | 32·0 | 48 |
| 4 | 0·7 | ,, 46–50 | 6·0 | 9 |
| — | — | ,, 51–55 | 0·60 | 1 |
| 555 | 100 | Total | 100 | 150 |

The defective was the only child in 10·26 per cent, the last child in 22·5 per cent of the cases, while the corresponding figures among Mongol children were 10·56 per cent and 61·38 per cent respectively. As to the size of the family, I found no appreciable difference in my two samples.

Ill-health of mothers, anxiety, worry, fright, various physical ailments including infectious diseases such as rubella during pregnancy, shocks, falls, ill-treatment, premature births, twin births, instrumental deliveries and other possible or assumed causative agents, figure among my cases just as they are to be found in the numerous statistics of other investigators. They do not call for special comment. The possibility of defect due to rhesus incompatibility of the blood of mother and foetus was not investigated. There is, I understand, considerable controversy on this subject in the literature.

Let us now consider the findings in the sample of 150 Mongols. Evidence of heredity was present in 34 of these cases. Just as in ordinary defectives and, to a smaller extent, also in normal individuals, defectives could be found among nearest relatives, sometimes another Mongol. There were many instances of one of the parents now being an inmate of a mental hospital, or grandparents, uncles

and aunts having been in institutions. The picture, however, differs in so far from that in ordinary defectives that these 34 represent only 22·7 per cent of all cases against 66 per cent in ordinary defectives, a ratio of 1 : 3. Even of these 34 cases more than half of the mothers presented so convincing additional evidence of environmental causation such as very advanced age, large interval between pregnancies or a long series of children before the birth of the Mongol, that I personally feel inclined to consider the hereditary factors as concomitant only as I would do with hereditary factors of deficiency or insanity in normal persons, and to credit environmental factors as being the causative agents. I am far from denying that hereditary factors may in some way or other be instrumental or play their part in the production of the Mongol, but theirs can only be a secondary role. Where one or another environmental factor has caused serious damage to the uterine mucosa and so laid the foundation to the Mongoloid malformation, genetic elements may prove to be very serious additional contributory factors, but I very much doubt whether they would have caused this special type of defect without the initial damage due to exogenous influence.

Compared with the evidence of heredity in my sample of 150 cases, evidence of environmental causation is far more common.

In 21 cases the mothers had a curettage prior to the conception which resulted in the birth of the Mongol, i.e., 14 per cent against 1·26 per cent in the ordinary defectives. In some of them as many as two or three miscarriages preceded the birth of the Mongol, partly brought about by the intake of abortifacients, and partly by irrigations with irritant solutions, but in all these cases the last miscarriage had always been due to curettage. In one case the interval between the curettage and the following pregnancy was only six weeks, in another ten cases from three to six months. Only in five cases did the interval exceed half a year, but was always less than one year. The curetted mothers were either very young and did not wish to have a child yet, or they were rather advanced in age and wanted to prevent a further addition to their already large number of children.

In addition to these 21 cases of confirmed curettage, there were :

9 abortions, brought about by the use of abortifacients,
6, where mothers stated that a severe fall or shock had propagated the miscarriage,
6, where a so called spontaneous abortion had occurred in mothers of rather advanced age. In three of these cases a stillbirth had preceded the miscarriage. Eventually there were
11 more cases in which I was unable to elicit any reasonable explanation for the abortion, where, however, the mothers left me in no doubt that a severe haemorrhage had occurred shortly before the conception. It is not to be excluded that some of these mothers were unwilling to admit a curettage or the intake of abortifacients.

Altogether we therefore have another 32 miscarriages to add to the curettage cases, making a total of 53, or 35·5 per cent, where the preceding miscarriage, at least in my opinion, had caused enough damage to result in the birth of a defective child. This figure compares with only 4·32 per cent in the sample of ordinary defectives.

I am unable to state how long a time had elapsed between the miscarriage and the birth of the Mongol in all instances, but more than half of them were pregnant before two to six months had elapsed after the abortion.

I personally feel convinced that in all these cases the uterine mucosa had not recovered completely from the mechanical, chemical or any other damage inflicted upon it, and that the ovum, therefore, had embedded itself in a vulnerated, lacerated or inflamed mucosa which was unable to provide the necessary nutrition for the growing embryo.

In this connection I must mention several other instances where serious impairment of normal uterine and nutritional conditions must have existed.

Four mothers were suffereng from a severe uterine and vaginal prolapse before the conception which ended with the birth of the defective child. In one of these cases there was persistent pain and vaginal discharge during the whole pregnancy, two of them were operated on shortly before the conception, one was complicated by frequent suppression of urine. One mother was found to be suffering from a fibroid growth of the uterus immediately after the confinement ; another died

of a carcinoma of the uterus two years after the birth of the Mongol. In these two cases some pathological changes must have been present already at the time of conception. A third mother had an ovarian operation and a uterine abscess shortly before she became pregnant. It was a premature seven months' child. One mother had an operation performed on her in order to enable her to become pregnant. Her only following pregnancy at the age of 37 years terminated with the birth of the Mongol. Two other mothers received prolonged treatment by injections in order to be able to conceive. In both cases their only children were Mongols, the mothers ages being 39 and 40 years respectively. In five instances there occurred from one to several haemorrhages in the course of the pregnancy, requiring longstanding rest in bed and treatment by injections. In two of these cases the mothers were relatively young, 21 and 26 years respectively. Their menstruations had been very irregular prior to this their first conception. The subsequent children were all normal. The other three mothers were 38, 41 and 43 years respectively. Three more mothers are worth mentioning : they had taken large amounts of quinine in order to procure abortion. They had had intermittent pain and a serous, partly haemorrhagic discharge in the course of the later stages of their pregnancies, but no abortion had followed. They were all approaching the age of 40 years. In this latter connection I would like to draw attention to a paper by P. Desclaux on the possibility of quinine intoxication during pregnancy being responsible for Mongolism. Eventually one mother should be included in this series. She had had a miscarriage at two months—by the way, this case is not mentioned among the miscarriages before—and was very ill in hospital for 14 days. She was subsequently discovered to be still pregnant, having had either twins or an incomplete miscarriage. Her age was 35 years.

In these 19 cases, or 12·7 per cent, there must have existed either at the time of conception or shortly afterwards, perhaps even persisting throughout the whole pregnancy, a serious impairment of the organs of generation, necessarily influencing the nutritional supply to the embryo. These 12·7 per cent compare with only 3·24 per cent in the sample of ordinary defectives.

Many writers have drawn attention to the fact that a large interval between pregnancies may easily lead to the birth of a defective child. Van-der-Scheer found that in 28·5 per cent of his cases such a gap of from five to seventeen years had existed. Still, Myers ,Jenkins, Hill and many others were strong supporters of this view. In my monograph on Mongolism I have pointed out that during such a long interval, especially when the mother is approaching her menopause, the uterine mucosa most likely undergoes changes bringing about a return to the primary condition of infantile development just as it existed before she reached maturity, and that a pregnancy taking place after the elapse of such an interval may easily terminate with the birth of a Mongoloid child.

In 43 of my 150 Mongols such a gap had existed ranging from six to seventeen years. Of these 43 mothers, not less than 19 were forty years or over, and in 21 instances the interval was 10 years or over. In quite a number of these cases we have, therefore, in addition to the physiological shrinking and degeneration of the uterine mucosa due to advanced age, the regression of the mucosa to infantile condition due to the elapse of so long a time between the pregnancies. These 43 cases represented 28·80 per cent of the total. If we therefore agree that—

53 cases, or roughly 35·5 per cent, had a miscarriage by curettage or other means,

19 cases, or 12·7 per cent, an impairment of the organs of generation at the time of conception or shortly afterwards, and

43 cases, or 28·8 per cent, an interval between the preceding birth and that of the Mongol of from six to seventeen years,

we arrive at a figure of 115 cases, or 77 per cent, in whom a pathological uterine condition stands out so clearly that it would seem to me futile to look for any other causative factors.

I must admit, however, that this figure is slightly in excess of correct statistical facts, as in some of these cases there existed an overlapping of miscarriage and time-interval, or miscarriage and rather advanced maternal age plus frequent pregnancies prior to the Mongol. If these cases are excluded from the statistical point of view we arrive at a figure of 98 cases, accounting for 65·66 or say roughly 66 per cent.

There now remain 52 cases or roughly 35 per cent to be considered for a plausible cause of this specific deficiency. Before doing so, just a few words about the ages of the mothers at the time of the birth of the defective, and the size of the family :

4 mothers, 2·7 per cent, were below the age of twenty years, as a matter of fact, not yet eighteen,
41 mothers, 27·3 per cent, between 20 and 35 years, and
105 mothers, 70 per cent, between 36 and 55 years.

If we agree that before the age of twenty years the uterine mucosa may still be in an infantile stage of development and not afford ideal nutrition, only 27 per cent of the children were born during the optimal child bearing period of the mother while 73 per cent, in other words more than two-thirds, outside this range. One look at the attached table clearly shows the enormous difference in that respect between ordinary defectives and Mongols : in ordinary defectives 76·6 per cent of the children being born during the optimal child-bearing period, in Mongols 27 per cent only.

The close relationship between advanced maternal age and increasing number of Mongol children has been stressed by many writers in the past. Only recently Penrose has again emphasized the enormous aetological importance of maternal age. To quote his own words, " Up to the maternal age of 34 years the chance in the general population of the birth of a mongoloid child is less than one per thousand, between the ages of 35 and 44 years the chance is nearly one in 200, and after 45 years it rises to one in 40." He then comes to the conclusion that the " evidence of hereditary influence is scanty and difficult to interpret."

As to the size of the family : the Mongol was the only child in 16 cases = 10·72 per cent. In 13 of them the mothers were beyond the optimal child-bearing age, 31 came from families of 5 to 7 children, 16 from families of 8 to 10 children, and 17 from families of 11 to 16 children. Thus 64, or 42.9 per cent came from families of from 5 to 16 children. We must agree that in all these cases the uterine mucosa had been subjected to damage and scarring of a lesser or greater extent in the past.

The Mongol was the last in a series of children in 93 instances, = 62·31 per cent. Added to these the 16 only children, we find that in 109 cases, or 73 per cent, there was no further pregnancy after the birth of the Mongol.

Let us now return to these remaining 52 cases. Of these the Mongol was one of twins in three instances, the twin brother or sister being normal. In 37 cases the rather advanced age of the mother and a large number of preceding pregnancies with their unavoidable changes in the uterine mucosa, in some instances coupled with severe emaciating disorders at the time of conception or during the early stages of the pregnancy, justify the assumption of a detrimental influence upon the placental circulation and upon the nutritional supply to the embryo. In one case the mother was suffering from rubella in the sixth week of pregnancy. Mongolism as a consequence of maternal rubella was first mentioned by Gregg. Ingalls and Davies found that in six of their seven cases the mothers had suffered in the early stages of their pregnancies from rubella, mumps, influenza or other infections. On the other hand, Levy and Perry, in a comparative study of the mothers of Mongol and ordinary feeble-minded children, are reluctant to credit infectious disorders of the mother during the early stages of pregnancy with the causation of Mongolism.

A case that is not included in this series has been communicated to me recently. A mother gave birth to a Mongol boy at the age of 35 years. She had had two normal children before, and the Mongol was followed three years later by another normal child. There is no history of mental defect in the family. She had felt particularly well during pregnancy, and the confinement had been timely and normal. She stated that she had been in contact with cases of German measles in the early stages of her pregnancy, but that she had not contracted the disease herself. I wonder whether bacterial or toxic infiltration through the chronic barrier of the placenta is possible without active disease of the mother. She naturally may have overlooked a very mild or abortive infection of herself when in touch with these cases.

Twelve cases representing roughly 8 per cent of the Mongols remain unaccounted for.

These twelve mothers had been relatively young at the birth of the defective

child ; they had had two or three children only, partly preceding, partly following the birth of the Mongol. There was no miscarriage, no other pathological uterine condition, and there existed no large interval between the birth of the Mongol and the preceding pregnancy.

The mothers had all been healthy during the pregnancy ; they had had normal confinements, and continued to be in good health afterwards. As far as I was able to ascertain, there was nothing to indicate hereditary factors. They would not admit any mental disorder or any pathological aberration from the normal in any member of their families. I must further admit that many of these informants were of quite a high intellectual standard and very co-operative, so that these cases cannot be explained away with perhaps lack of understanding or misconstruction of facts. These 8 per cent represent that small fraction which we shall encounter in any phsyical or mental disorder, for which no reasonable explanation can be given—so far. We have yet to learn a great deal, and further research may enable us to find factors which would bring even this small fraction in line with all the other cases.

What then are the conclusions that can be drawn from this study?

In comparing the two groups, there is ample evidence of hereditary factors in ordinary defectives of all grades and in the various special types with the exclusion of Mongols, in whom genetic factors are negligibly small. The mode of transmission and the possible combination of genes in the various types of mental defectives is still far from clear, and it is for the specialists in this field to establish further convincing proof of their inheritance theories. I have no hesitation in acclaiming their enormous progress in recent years.

Environmental causation can be satisfactorily established in quite a number of ordinary defectives but is overwhelming in Mongols ; as a matter of fact, with the exception of approximately 8 per cent of the cases, extrinsic influence is evident in all of them. This brings to mind the views so often expressed in the literature, namely, that mental deficiency is not a uniform disorder, and that a great variety of agents, either alone or in combination, contribute to its causation, while Mongolism as a specific type of defect cannot be due to multiple, but to one single cause alone.

Among the environmental factors we find that miscarriages brought about by curettage, by abortifacients or by other means and other pathological uterine conditions were responsible for 7·5 per cent of the ordinary defectives compared with roughly 48 per cent in Mongols. If we add those cases where there existed a large time interval between the two pregnancies, where mothers were very advanced in age or had had a large number of children before, and where no other causative agents including heredity could possibly be blamed, we might easily conclude that from between 12 to 15 per cent of ordinary defectives owe their pathological mental condition to uterine factors, compared with 92 per cent in Mongols.

We have, therefore, two entirely different groups of defectives to deal with from the causation point of view. In the ordinary defectives hereditary factors alone, or environmental factors of different kind alone or a combination of the two may be active to bring about the deficiency. As to Mongols, ever since the classification of defectives according to ethnical groups by Langdon-Down, numerous theories have been propagated by a host of writers in the past. It certainly is unnecessary to recall all of them as so many, though very interesting and in a way perhaps acting as " pathfinders," cannot longer be taken seriously into consideration. They have been dealt with in my previous papers and in my monograph on Mongolism, and those that are particularly interested are referred to the latter. The subject still remains a very fascinating one, as hardly a month elapses even now without some contribution to it. Out of the variety of theories, that of hereditary causation is still strongly discussed and disputed by a number of workers. On the strength of many studies, my own among them, there is no justification to uphold a genetic aetiology of this disorder, but may I be allowed to emphasize again that I am far from denying heredity its place as a causative factor also in Mongolism. I am, however, of the opinion that it plays a secondary role only.

Horst Geyer strongly favoured a plasmatic disorder due to ovarian insufficiency, and still has some supporters.

Benda, who has carried out extensive research and whose publications are certainly of a very high scientific standard, ascribes Mongolism to a threshold con-

dition of hormonal sterility of the mother—in other words to a pituitary dysfunction. His pathological findings are, however, far from convincing, and all attempts at a substitution therapy have entirely failed.

The present investigation has only strengthened my belief, expressed already in the past, that a pathological state of the uterine mucosa alone must be responsible for this deplorable physical and mental abnormality. In a number of cases genetic factors may cause havoc after an initial damage through extrinsic elements.

Odd as it may appear at first sight after my previous statement, Benda is, to a very great extent, quite right when he blames the pituitary gland as being the responsible culprit. His mistake lies in the fact that he blames the wrong pituitary, namely that of mother instead of that of the defective child. On account of poor nidation and consequently poor nutrition, there is inadequacy of development of many embryonic tissues, among them of the endocrine glands. No doubt, the pituitary of the child is grossly affected, which easily accounts for the stunted growth and many other stigmata of the Mongol. I fail to understand how a deficiency of the maternal pituitary could result in these malformations.

I feel inclined to overlook the few cases in which proof of my view could not be established. Further research on these lines in the near future may give a more satisfactory answer for these cases as well. The observation that a number of ordinary defectives show no other causative agents than a vulnerated or degenerating uterine mucosa with its pathological placental circulation should encourage students to consider the uterine factor as a possible and very potent causative element in a percentage of cases of ordinary mental defect as well.

I am indebted to Professor Penrose for advice and healthy criticism.

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# A COMPARISON OF THE PSYCHOLOGICAL EFFECTS OF DIFFERENT TYPES OF OPERATIONS ON THE FRONTAL LOBES.*

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## Personality Changes Three Months after the Standard Operation.

Three years ago at the last International Congress of Psychology I reported on a preliminary investigation of personality changes after the usual standard prefrontal leucotomy. This investigation was carrried out on 20 neurotic patients before and three months after the operation performed by Mr. McKissock (McKissock, 1943). An extensive group of objective personality tests were chosen to define the factors of " Neuroticism " and " Introversion " as described by Eysenck (1947), which to all intents and purposes are equivalent to Cattell's (1950) factors C and F. In addition, the following intelligence tests were used : the Wechsler Scale, Porteus Mazes, and the proverbs from the Stanford Binet. The changes found provided us with some evidence in support of the hypothesis with which the investigation had been planned. This was that as a result of this type of incision in the frontal lobe there was a decrease in " Neuroticism," a decrease in " Introversion " and a decrease in certain aspects of intelligence (Petrie, 1949*a*).

Since then a further 50 patients have been examined before and after operations on the frontal lobes, bringing the total to 70. Most of these were severe neurotics attending the psychiatric department of Dr. Desmond Curran at St. George's Hospital, London. Only those changes will be referred to as an alteration in personality where the probability is less than one in twenty that they could have occurred by chance.

## Personality Changes Nine Months After the Standard Operation.

We have examined patients for a second time after a longer period—approximately nine months after the operation—and these results show that the constellation of personality changes after the standard prefrontal leucotomy remains the same after the longer interval, some of the changes in personality becoming more accentuated as time goes on (Petrie, 1949*b*).

## Personality Changes After an Operation Anterior to the Standard.

We have also investigated a patient operated on by the same neurosurgeon—Mr. Wylie McKissock—but using a more anterior incision in the frontal lobes than that made in the standard approach (McKissock, 1949). This anterior incision, called rostral leucotomy, differs from the more posterior one in that the destruction involves as much as 50 per cent. less of the prefrontal region, areas 9 and 10 being primarily affected (Meyer, 1951).

After this anterior operation the pattern of significant changes in *temperament* and *character* is the same as that found after the posterior operation. These changes are, however, less pronounced after the anterior incision.

Thus after both types of operation the patients display decreased suggestibility, decreased perseveration, increased manual dexterity and tempo of handwriting and less self-criticism—all of which indicate a decrease in the factor of " Neuroticism."

They also display a tendency to work at greater speed and more inaccurately at both mental and manual tasks, a tendency to blame the environment rather than themselves both for personal character deficiencies and their failures—they become in Rosenzweig's (1944) terminology less Intropunitive. They show a preoccupation

* This paper was read to the 13th International Congress of Psychology, held in Stockholm on 19 July, 1951.

with the present rather than with the past and the future, an increased liking for sex humour, and the ratio of their verbal intelligence to their performance intelligence scores has dropped. These changes indicate a movement away from the Introverted end of the scale (Petrie, 1950).

### Difference in Effects of Posterior and Anterior Incisions.

These are the similarities between the effects of anterior and posterior operations. Now let us consider the differences. I have mentioned that there was a loss in certain aspects of intelligence after the posterior operation ; in fact, both in the early and later investigations significant losses in the Wechsler I.Q. were found, particularly on the Verbal Scale, in Porteus Mazes Mental Age and in the ability to generalize displayed in interpreting the proverbs.

There was also after the posterior operation an alteration in the use of language found both in spoken and written material. Words were misused to cover an area of meaning for which they were not normally intended. For example a patient of superior intelligence suggested that a nail was a "*metal joiner*"; another of good intelligence proposed that fur could be used as a "*wearing apparatus.*" One woman with a First Class Honours University degree wrote that she will never forget her aunt's "*straight-sitting attitude to sexual illusions,*" and a more extreme example came from a woman of average intelligence who stated that brave meant "*to show good taste.*" This strange use of language was, of course, only shown after the operation, but persisted after an interval of years.

None of these changes in the intellectual aspects of personality present after the posterior standard incision were found after the anterior incision. The anterior operation appears therefore to achieve the personality changes whilst avoiding the effect on intelligence of the posterior incision (Petrie, 1951).

I have stated, however, that the extent of the alteration in personality was less pronounced after the anterior operation. It is probable that for some of the patients the personality change caused by the anterior incision was insufficient to be therapeutically successful, for the clinical assessments of the posterior and anterior operations indicated that the latter achieved the greatest clinical success.

### Difference in Effects of Left and Right Incisions.

I had the opportunity of comparing the personality changes in four patients operated on the right frontal lobe only with those in four patients operated on the left frontal lobe only. These were all right-handed people. There were among the results some indication of a difference between leucotomy on the right and left side. Although the numbers are so small, it was very noticeable that the pattern of changes in those operated on the left was closer than that in those operated on the right to the effect of a bilateral operation. This suggests that the left frontal lobe may be contributing more than the right to the personality changes following on these operations. Neurologists are aware of left dominance as far as speech centres are concerned ; perhaps our results hint at *left* dominance in other spheres, including the part which the frontal lobes play in the determination of personality (Petrie, 1952).

### Open and Closed Operations.

Some evidence was obtained of the desirability of open leucotomy. A group of patients who had the blind operation were compared with a group who had an open one. Although the personality changes were of the same pattern after both these approaches, the standard deviation of the changes after the blind incision were greater than after the open one. This greater variability after the blind incision supports the belief that one of the advantages of the open operation is its greater precision (Meyer, 1950).

### Social Attitudes and the Prefrontal Areas.

An association between social attitude and the frontal lobes was suggested by some of the results. It was mentioned that there was a loss in Verbal I.Q. of the Wechsler after the standard operation. This was almost entirely due to lower scores on one of the four tests used—the Comprehension sub-test. This consists of ten questions ; it was found by three independent judges that the answers showing the greatest loss grouped themselves to cover an area concerned with social attitudes. They included the importance of keeping promises, the appropriate behaviour to

prevent train accidents, the importance of a fair distribution of Government appointments and of charity. The special loss in social attitudes was found both at the earlier and the later investigations, and confirmatory evidence was noted in the essay written by patients about themselves and people they liked and disliked—in which socially desirable qualities were less frequently referred to.

After the anterior operation there was no loss in total score of the Comprehension sub-test, but an examination of the 10 individual answers showed that there was a significant gain on one of them and a significant loss on another. The gain was in answering the factual question about the reasons for cotton being suitable in the making of cloth, the loss was in the answers to " Why should a promise be kept ? " It would appear that this is a suggestion of the same type of change noted after posterior leucotomy, a loss involving especially social attitudes.

These various findings may be supplying a hint of the social functions of the frontal lobe. We have noticed, for instance, that following on the incisions in these lobes there is less feeling of personal responsibility and a strong tendency to direct criticism outwards ; the patient is more satisfied with himself, his activities, his style of living and doing things ; he is less concerned with getting things quite right and is more slapdash and inaccurate. He likes sex jokes more, and even the carelessness in the use of the language may be related to an aspect of conscience, as Stengel (1939) and others have suggested.

One of the major differences between the brain of a man and that of a chimpanzee lies in the development of the prefrontal region—the most anterior part of the frontal lobes (Penfield, 1950). It is of interest that Turner's (1948, 1950) studies of the development of the frontal lobes in the life-history of Man indicate that both in size and complexity the period of maximum growth is later than that of the rest of the brain. Moreover, the frontal lobes have a period of intensive growth between the ages of two and five. If the frontal lobes do constitute in normal conditions the area for the functioning of what is commonly called conscience, the time of their development may be related to the psychoanalysts' observation that the super ego, controlling social behaviour, develops round about the age of five.

## Pain and the Prefrontal Areas.

Leucotomy is also used for the relief of intractable pain, but how the relief is obtained is puzzling, for numerous researches have shown clearly that the threshold for pain is not higher as a result of the operation ; in fact, if there is a change the patients are *more* sensitive after leucotomy to immediate painful stimuli (Chapman *et al.*, 1948 ; Le Beau and Pelker, 1950). Leucotomy however *does* relieve the suffering of a patient with inoperable cancer—example, Fleming, 1950. Although none of the cases on which I am reporting were leucotomized for pain, our results may throw some light on how the operation achieves this end.

In addition to the changes on the variables I have already mentioned, the tests used demonstrated that after leucotomy time passed more quickly for the patient, they were more distractible, and they showed increased control in the fluctuation on an ambiguous figure.

These three changes—and the alteration in attitude to the past and future reported earlier—may be contributing to the decreased suffering of the patient who has had a leucotomy for pain in the following ways :

Firstly, the painful situation may become more bearable by reason of the increased distractibility of the patient, who finds it easier as a result to be distracted from his painful situation by what is happening round him. Secondly, we have noted that after the operation the patients are more orientated to the present than to the past and future. Hence in so far as the past and future components contribute towards the total painful situation, this may also have been diminished. Thirdly, if time is passing more quickly for the patient, whatever the present may mean in terms of his suffering, it is more quickly over. And finally, the control in the fluctuation of an ambiguous figure (the Necker Cube) has been shown by Gordon (1950) to be related to control of imagery. Those who show less control in the fluctuation have the more vivid imagery. This suggests that our patients have less vivid imagery after the operation. In a normal adult there is no doubt that the experience of pain is compounded of the perception of present pain, and the imagery of the pain that is gone and the pain that is to come. If the post-leucotomy patient has indeed less vivid imagery, and as a result both the memory and anticipation of pain is less real, this would also contribute to his decreased preoccupation with his own suffering.

Summary.

The main points I have tried to make will be briefly summarized. After both an anterior and posterior incision in the frontal lobe, the pattern of significant changes on an extensive group of objective tests of temperament and character is the same, and indicates a decrease in the factors of " Neuroticism " and " Introversion." These changes are, however, more pronounced when the operation is more posterior, but intellectual loss is only found after the *posterior* incision. There is some indication of left-dominance with regard to personality changes.

In connection with the use of the operation for the relief of intractable pain, some suggestions have been put forward as to how this may be achieved. Finally, I have tried to draw attention to the fact that there is more than a hint in the results that the frontal lobes may be subserving very important social functions in man.

My thanks are due to Dr. Desmond Curran for permitting me to carry out these investigations in the Psychiatric Department at St. George's Hospital, London, and to the many members of the medical and nursing staff who assisted in various ways.

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# SOME FURTHER OBSERVATIONS ON HEAD-BANGING AND ALLIED BEHAVIOUR.

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In a paper published in the *Journal of Mental Science* for July, 1950, I suggested that head-banging originated in the infant's desire to reproduce the thrust of the mother's apex-beat against his head while he was being nursed on her left arm, either as a means of self-comfort or in retaliation for what he had felt to be an attack or as both combined. In the present paper I propose to analyse this infantile experience further, and to trace to some of its component elements certain other peculiarities of childish behaviour.

I shall begin by considering the case of a bottle-fed baby, that is to say, one who at *every* feed is held in his mother's left arm with his right temple against her left breast (and I shall suppose that the mother is not herself a case of dextrocardia.) In addition to the teat in his mouth and the milk being swallowed, such an infant feels the thrust of the mother's apex as a series of taps against his head which tend to impart to the latter a rolling side-to-side movement, he hears her heart-beat as a rhythmic lub-dŭp, he feels the rise and fall of her chest in respiration as a slower to and fro rocking of his whole body, and he hears the sighing rustle of her breathing beneath his ear. The sound and thrust of the heart-beat are of course louder and stronger at the limit of the mother's expirations, and indeed the tap of the apex may be felt only then. In other words, the suckling hears two separate series of interwoven unsynchronized rhythmic sounds continuing throughout the whole of his feeding times. In addition to all this, he feels the warmth of the maternal body, the steady clasp of the mother's arm, he smells the milk and the woman's body odour (sweaty, or scented by her soap and talcum powder), and lastly, he feels (and may smell) her breath as an intermittent warm breeze on his face and in his hair. The mother seldom speaks while she is feeding her baby, and the room is often quiet, mother and child being alone together. A breast-fed baby also feels smooth warm skin under his fingers, but he has the mother's heart against his head, during only half his feeding times.

The other occasions on which a woman commonly holds a child firmly against her breast are, of course, when she is trying to comfort a crying baby, or to restrain a struggling toddler from escaping to some forbidden activity. Here the child is angry and the mother herself often either anxious or angry or both, so that her heart-beat is greatly increased in force, and the furious infant feels it as a series of aggressive blows on his head, each of which is accompanied by a bumping noise.

## Attempted Reproductions of the Nursling Experience: Imitation as a Means of Self-Comfort.

I shall begin with the good feeding situation, and consider first the infant's experience in it as a whole. To the suckling this experience represents the greatest possible satisfaction of his desires, and therefore the state of greatest possible content, so that it is natural that in later life when he feels the need of comfort he should try to recreate that early situation. However, the experience does not only contain the seeds of future nostalgia, but also, perhaps, memories of a previous state. The new-born baby held against its mother's left breast after feeding comes nearest to recapturing the conditions of his recent antenatal life. How much an infant of a few days old can possibly remember the anatomists and physiologists may one day be

able to state with certainty and precision, but we already know that the infant begins to learn in very early life, and for learning memory is essential, so that it seems possible that enough may be remembered of antenatal conditions to give rise at least to a sense of familiarity, and therefore of security and content, when early post-natal experience approximates to that previous state.

The foetus *in utero* floats in warm amniotic fluid, which maintains an even gentle pressure over most of his skin surface. All his needs of food and oxygen are met without effort on his part, and therefore without his needing to experience desire (a state approximating to Nirvana, one must suppose). He is in darkness, but not in silence. The sound and thrust of the pulse in the mother's abdominal aorta, in front of which the uterus is lying during the later months of pregnancy, must be clearly transmitted to the amniotic fluid as sound and pressure waves. In place of the rise and fall of the maternal chest in respiration experienced by the suckling, the foetus experiences an up and down tossing and swinging movement when the mother walks, and in place of her respiratory sounds beneath his head, the peristaltic sounds round about are probably audible *in utero*.

To return to firmer ground, however, Margaret Mead observed (1) that thumb-sucking occurred in children who had had feeding difficulties during the earliest months of life. From the small series of cases I have so far collected, I would say tentatively that head-banging as a means of self-comfort appears to occur in certain children who are too abruptly weaned, or who are deprived of their mother or of her attention at about the time of weaning. I give a brief extract from the history of such a case.

ALEC: This child was brought to the Chatham Child Guidance Clinic. He had been bottle-fed from birth (which was normal). He had been an 8½-lb. baby and "good" till three months old, but thereafter used to cry between feeds by day till eighteen months old. Until he was eight months old his mother held him on her lap to feed (she is right-handed), but after that she sat him in a high chair for his feeds. He was weaned from the bottle by eleven months old. At eight months old Alec developed the habit of banging his head backwards against the chair when he was first placed in it (that is, before his meal began) as long as his mother was in the room, but always stopped if she went out or moved to where he could no longer see her. He lost this habit at about the age of eleven months, that is, when he ceased to be fed from a bottle.

This case shows clearly the association in the child's mind between suckling and the banging on the back of his head. He tried to expedite the start of his feeds by himself providing the right accompaniment, when his mother herself ceased to do so, as soon as he saw that she was present.

The commonest spontaneously adopted method of reproducing the nursling's situation is, I think, for the child to rise on hands and knees in his cot, and to rock backwards and forwards in that position, bumping his head into the pillow at the end of each forward thrust. Sometimes he also makes a rhythmic humming noise as well. (In the case I reported in my previous paper the boy imitated the sound of the German V1 bombs, the "doodles," and in another case I saw at the same Clinic the child, whose mother had formerly made a practice of singing to him while holding him in her arms, used to sing to himself while rocking and banging in this way). As the child grows older this habit often gives place to head-rolling on the pillow. I had recently a twelve-year-old boy under treatment at the Chatham Clinic who had been a head-banger till four or five years old, and who used to roll his head rhythmically from side to side while sitting drawing in silence in my room—an occupation which he loved.

The next commonest method of reproducing the longed-for situation seems to be by rocking in a sitting position. I have been told by a friend that when her husband visited several Displaced Persons' Camps in Germany after the war, he was struck by the fact that the younger children all had the habit of rocking to and fro as they sat, and he was informed by workers that this was the habit longest retained after the children had been adopted into private families. He was also told that some of the children had been taught to clap their hands (a German way of expressing "please" in infancy, I learn), and that if someone sang to them, these children would sit and rock to and fro, clapping their hands twice at the end of each forward swing of the body. It is of course well known that rocking with the thighs pressed together is a common method of masturbation in infancy, but it does not appear that all, or even most, of these children were masturbating in the strict sense of the word, that is stimulating the external genitalia, though it is obvious that they were

comforting themselves, and I suggest that the comfort was derived from the simulation of their old nursling situation.

A third method of achieving the same thing I have heard described only at second hand : a little boy greatly puzzled his parents by developing the habit of rocking from side to side in a standing position, clapping his hands twice near his right ear after each swing to the right.

Before leaving the subject of rocking, it is worth recalling that until recently babies were put to sleep in rocking cradles, and that even now mothers instinctively rock their children in their arms to soothe them, reproducing fairly closely, I imagine, the type of movement felt by the foetus *in utero* when the woman is walking. Nor is it only small children who find comfort in movements and sounds suggesting those experienced at the breast. A hammock swinging in the garden on a warm day with the breeze rustling intermittently in the leaves, a rocking chair in front of a purring fire with a clock ticking on the chimney piece, a hammock slung within a ship as she rises and falls on the waves with the distant throb of the engines or creak of the rigging audible, all these give a feeling of safety and drowsy content to their adult occupants.

### Head-banging as Angry Retaliation for a Seeming Attack.

Into this category fall those cases of head-banging by angry toddlers in which the child beats his forehead against the floor, wall, or furniture when he is in a tantrum, his fury increasing with the pain of each blow, since that pain itself seems to him his mother's present retaliation for his own attack. This type of banging is particularly disturbing to mothers, partly because they fear the child will really injure his head or even his brain, or that the habit is itself a sign of insanity (though this is not often openly admitted at first), but partly also, I think, because the mother does realize, without putting that realization into words, that the child's action is intended as an attack on herself. She may even be chiefly disturbed by her own emotional reaction to this knowledge.

### Exaggeration of the Maternal Apex Beat, Real or Apparent.

I have collected six cases so far in which exaggeration of the force of the maternal apex beat, either real or apparent, was followed by the development of head-banging in the child.

*Real exaggeration* may be either functional and intermittent, or organic and (usually) persistent.

Functional increase in the force of the mother's heart-beat occurs of course in anger and in fear. In the case I reported in my earlier paper the mother was very much afraid of the V1 air raids, and during alerts used to sit alone in the shelter with the child on her lap clasped to her breast by her left arm. The boy himself was not at all frightened, and he later developed the habit of banging his head backwards against the wall when sitting in his high chair, making a noise suggestive of the " doodles " all the while (as mentioned above).

Two most interesting cases of head-banging in the same family reported to me by Dr. Stephenson of Vancouver illustrate the development of the habit in children whose mother's heart beat was greatly increased in force as a result of organic cardiac disease. I quote, with his permission, part of Dr. Stephenson's personal communication, written from the Child Guidance Clinic, 455, Thirteenth Avenue West, Vancouver :

" We have lately seen three siblings, two of whom showed the symptom of head banging. . . .

" The children's home has been a battleground for the parents. They have often witnessed and experienced physical brutality on the part of the father when drunk. They all show gross signs of anxiety and emotional disturbance.

" June, born February, 1943, has sucked her fingers since the age of three months.

" John, born May, 1944, has banged his head against the bed at night since the age of six months. He had eczema as an infant. He is clumsy in his movements, having been coercively changed from left- to right-handedness. Relates poorly to other children.

" Allan, born November, 1946, bangs his head and hums in a monotone since the age of eleven months. Screams when startled or aroused from sleep. He is restless and distractible.

" The mother is right-handed and always cradled her babies in her left arm. The children were all bottle-fed. The monotonous humming of the youngest child drew my attention

since the mother is reported to have a cardiac lesion. I thought it would be interesting and strengthening to your theory should she prove to have a murmur. Accordingly I took the opportunity of listening to her heart and found that she had an abnormally forceful apex beat together with a rough, moderately intense apical diastolic murmur."

*Apparent increase* of the force and sound of the mother's heart-beat occur, one may suppose, in certain abnormal physical states of the infant in which there is hyperaesthesia. The commonest of these is, no doubt, otitis media. I have collected three such cases; in one the child's illness, diagnosed as meningitis, was followed by the appearance of an aural discharge a few months later, the second was a case of recurrent otitis media in a girl, and the third a case of concussion due to a blow on the vertex. I summarize part of the history of one of these as illustrating this group.

CHARLIE: seen at the Chislehurst Child Guidance Clinic. Full-term infant, normal birth. Breast fed till six months old. This boy was healthy until the age of two years; he then developed meningitis, was very ill for three days, and off his feet for two weeks, being nursed at home. Some two or three months later he began to have temper tantrums, which were accompanied by head-banging " on the floor, the wall, the table or sideboard, anything hard " nearby. About two months after this (his mother is a poor informant) he was found to have an offensive aural discharge, which persisted for several weeks. The head-banging during outbursts of anger continued till after he entered school at five years old.

To the child suffering from headache or earache, especially one with a tense and bulging tympanic membrane, even the slight concussion of the maternal apex beat (which may be increased in force either by the mother's anxiety or her irritation over the abnormal fretfulness of the infant, whose trouble is often as yet undiagnosed), even this tap must produce an exacerbation of pain at each beat, so that far from succouring him, his mother seems to him to be deliberately making his trouble worse, attacking him at the very time he most needs her help. Of the three children in the group just described, the first two developed head-banging of the purely aggressive type, that is to say, indulged in only during outbursts of anger, and the third (the concussion) that of a mixed, that is, ambivalent kind, all of them some months after recovery from the physical disorder, when presumably the unusual sensitivity to pain had subsided.

I think there is yet another mechanism by which aggressive head-banging may arise in children who have suffered from pain in the head or ears. In both otitis media and severe headache the patient's own pulse-beat may be felt as a throbbing fluctuation of his pain, and to the infant or small child who associated the throb of a heart-beat with being held against his mother's breast, it may seem that it is Mother who is now attacking him *from within* his head, and this in turn may lead to the development in him of retaliatory fantasies of his smashing *into* her with his head-banging.

I do not propose in this paper to enter into a consideration of the fantasies which a small child may evolve both to express to himself and to explain to himself his urge at times to rock and to bump his head, either when he feels lonely and in need of comfort or when he is angry with his mother, after the conscious memory of the nursling's experience has faded, but I have no doubt that such fantasies do arise in this way as well as in that just suggested above; their elucidation, however, falls within the province of analysis.

I would like to express my thanks to Dr. A. Elliott, County Medical Officer of Kent, for his permission to use case-material from the Chatham and Chislehurst Child Guidance Clinics.

REFERENCE.

1) MEAD, MARGARET: *Sex and Temperament in Three Primitive Societies.*

# PSYCHOLOGICAL CHANGES DUE TO E.C.T. AS MEASURED BY A BATTERY OF TESTS GIVEN REPEATEDLY.*

By Ralph Hetherington.

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## Introduction.

The majority of investigations into psychological changes due to E.C.T. have been undertaken to assess the effect of treatment on the patient's memory. Sherman, Mergener and Levitin (1941), testing for retention of material assimilated on the same occasion as it had to be recalled or recognized, found no significant effect of E.C.T. upon memory. Zubin and Barrera (1941) found that E.C.T. removed the saving that would otherwise have occurred between learning and re-learning paired associates. They also reported that the effect of treatment on the recognition of material was less severe than on its recall, and this was confirmed by Mayer-Gross (1943).

The present paper reports psychological changes which have been found to take place *during* a course of treatment with E.C.T. as well as before and after. The investigation is a development of a pilot experiment undertaken with Dr. M. Roth which was briefly reported at the International Congress of Psychiatry, Paris, 1950.

## Method.

The difficulties involved in repeating a battery of tests several times concern practice effects with material used repeatedly and transfer of training effects with similar material substituted in later sessions. These difficulties can largely be avoided by assessing the effect of E.C.T. on a learning curve obtained by the repeated use of a small battery of tests.

### *The Spacing of the Treatments and Test Sessions.*

The battery was given four times in all. The first test session was always given before the start of the course of E.C.T., either on the same day, or on the day before the first treatment. The second session was given the day after the fourth treatment, the fifth treatment taking place on the following day. In three cases this second session was given between the fifth and sixth treatments. The third session was given two or three days after the final treatment, and the fourth session ten days to a fortnight later. Eight patients received six treatments, one received five treatments and one ten treatments.

### *The Depressive and Control Groups Tested.*

The cases tested consisted of ten patients for whom the diagnosis was depression. There were nine women and one man, none below average intelligence (i.e., all with a score of at least Grade III on Progressive Matrices). The mean age of this group was 41·5 years (S.D. 7·7).

Two groups of people were used as controls. The first was a group of five male and five female nurses working at the Crichton Royal. Their mean age was 23·2 years (S.D. 5·6), and all had a Matrices Score of at least Grade III. This group was given the whole battery, except the tests of intellectual ability, four times at weekly intervals. They were not, of course, receiving treatment. The second control group consisted of fifty male A.R.P. workers, with a mean age of 36·9 years (S.D. 15·5), who were tested and re-tested in 1943 with the tests of intellectual ability at

* Based on a paper read at the Annual Meeting of the Royal Medico-Psychological Association, Dumfries, July, 1951.

an interval of about a month. These two groups being neither depressed nor undergoing treatment were not, of course, controls in the strict sense of the word, but were used to assess normal practice effects with the tests used.

*The Test Battery.*

The battery was designed to assess output of mental work, hand-eye co-ordination, speed of muscular work, and retentivity. It could be completed in less than 40 minutes. In addition, each patient was given a test of intellectual ability before the treatment started and again after the course was completed.

*Output of accurate mental work* was measured by asking the patient to add seven

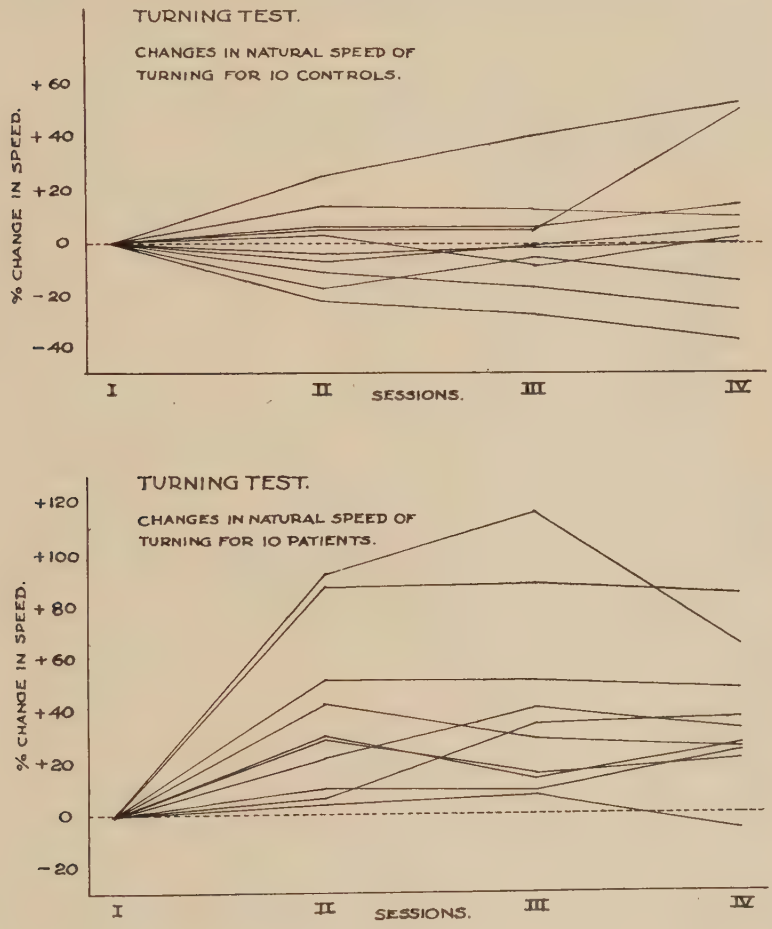


FIG. 1.

to each of a series of numbers printed on a sheet of paper. The number of sums accurately completed in three minutes constituted the score of the test. *Hand-eye co-ordination* was assessed by means of the Track Tracer (Vernon and Parry, 1949), and the total time taken to complete five runs constituted the score. The number of mistakes made on each run was also noted. *Speed of muscular work* was measured by asking the patient to turn a handle, first of all at his natural speed and later at his fastest possible speed. In each case the rate was recorded on a speedometer. *Immediate recall* was assessed by the Digit Span Test. *Immediate recognition* was assessed by asking the patient to select from a pack of forty cards those bearing names he had seen on a list of twenty names which he had studied for twenty seconds immediately beforehand. The number of cards accurately and wrongly

recognized were noted separately. The number of cards correctly chosen less the number wrongly selected constituted the score of the test. *Immediate recall and recognition* of non-verbal material was assessed by asking the patient twenty questions about a picture he had studied for three-quarters of a minute immediately beforehand. The pictures used were those of the Terman-Merrill revision of the

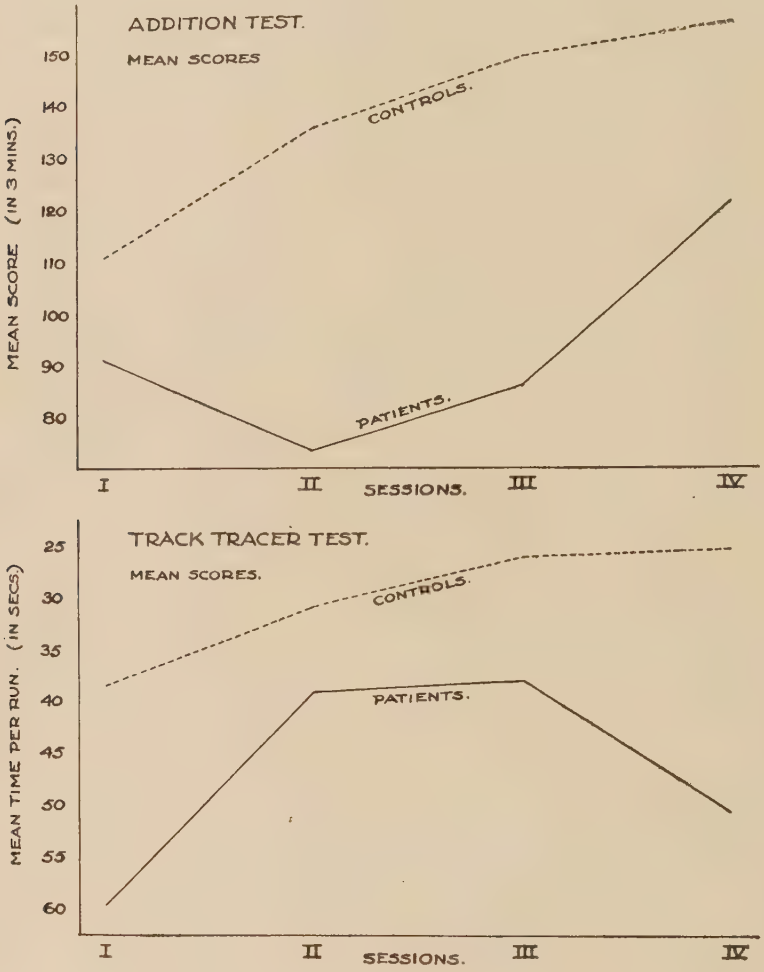


FIG. 2.

Stanford-Binet Test, numbered L. III–6, 4A, 4B, 4C ; M. III–6, 4B (Terman, Merrill, 1937). The number of questions correctly answered constituted the score of the test. *Recent recall* was measured by reading a short story at the first Session which the patient had to recall about ten minutes later. The story was " The War of the Ghosts " (Bartlett, 1932). It was then immediately read a second time. At each of the following sessions the same story had to be recalled, after which it was read once again. The number of statements correctly recalled constituted the score of the test. *Recent recognition* was assessed by asking the patient whether he recognized the pictures he had seen in previous sessions. He was also asked whether he recognized each test as one he had done the session before. *Intellectual ability* was assessed by means of Progressive Matrices and the Mill Hill Vocabulary Scale (Raven, 1948).

## Results.

In assessing the results of these tests the two main considerations are firstly whether there are any trends over the four Sessions in either of the groups tested, and secondly, whether there are any significant differences between the two groups at each session.

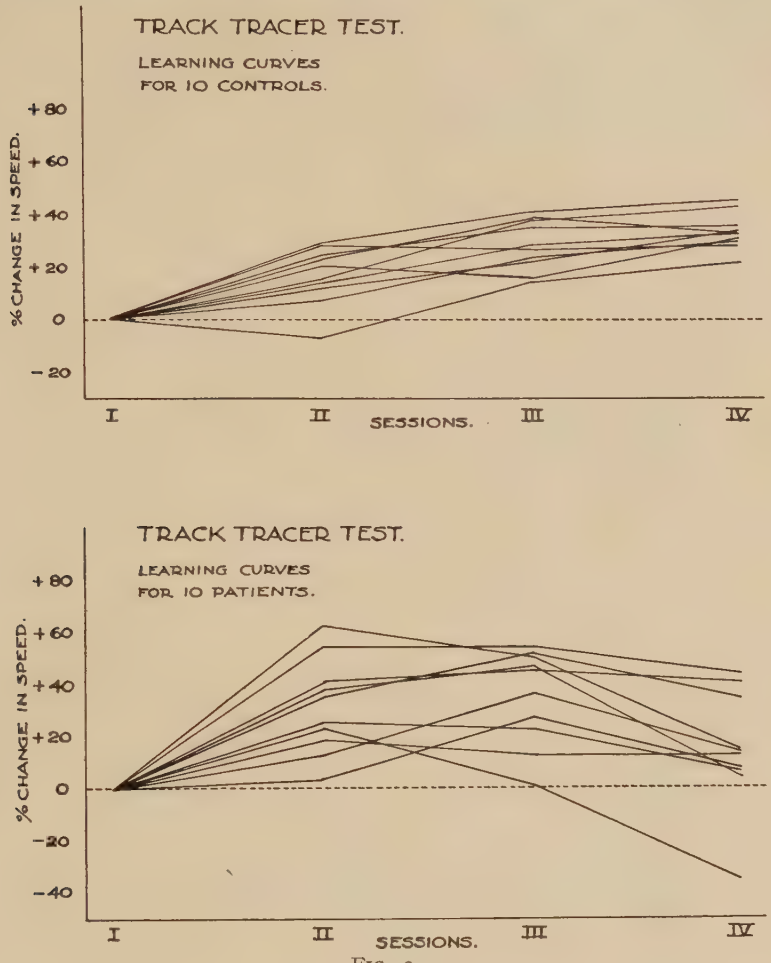


Fig. 3.

*Tests for Intellectual Ability.*

The increases in mean score in both *Matrices* and *Mill Hill Vocabulary Scale* for the Depressive group before and after the course of treatment were not statistically significant. There was no evidence of intellectual impairment before or after treatment as assessed by comparing the scores of the two tests. The mean scores of the Depressive and Control groups in both tests were statistically indistinguishable. It is interesting to note, however, that the mean time taken to complete the Matrices test in the case of the Depressive group both before and after treatment was significantly greater than the comparable mean time for the Control group.

*Tests of Efficiency.*

Some striking differences between the Control and Depressive groups were noticed with these tests. In the *Addition* test the Control group produced the expected learning curve. Nine out of ten patients produced a falling off of output of accurate work in Session II. This was followed by a normal learning curve in Sessions III and IV (Fig. 1). It is of particular interest to note that the one atypical

case which showed a more normal learning curve was the only member of the Depressive group who was markedly retarded, and was the one who produced the greatest percentage increase of speed (93·1 per cent.) in the Turning test between Sessions I and II (Fig. 3). It would appear that in this case the effects of the remitting psychosis outweighed the more usual effects of the treatment. The difference between the mean scores of the Depressive and Control groups was statistically significant in Sessions II and III (Fig. 4).

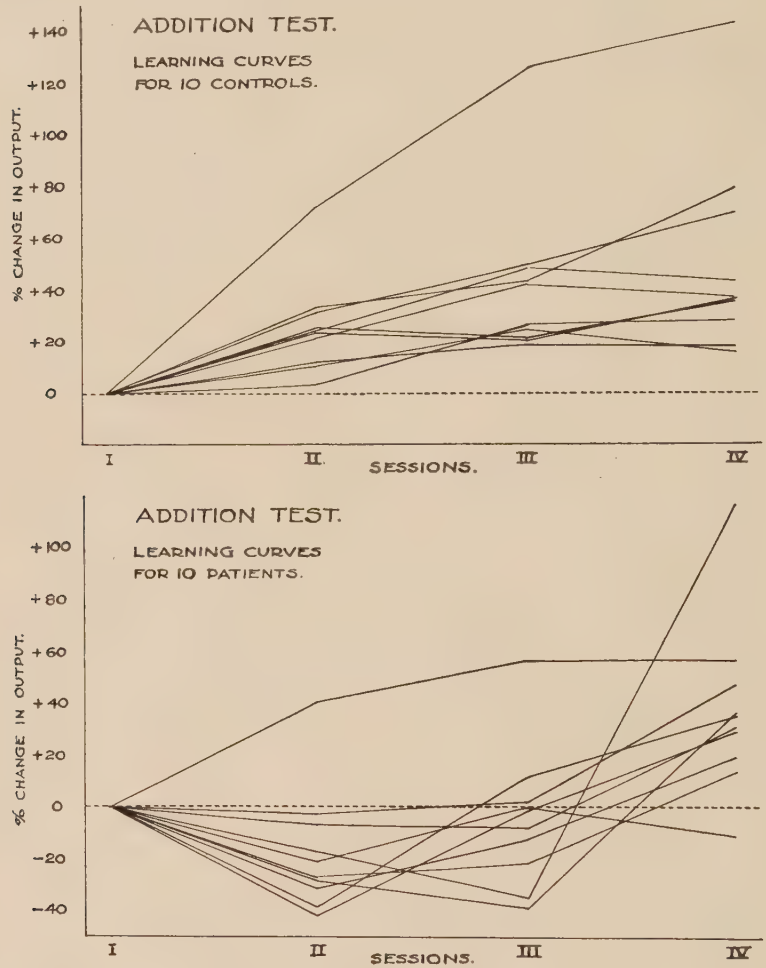


FIG. 4.

These results are in marked contrast to those obtained with the *Track Tracer* test. The expected learning curve for speed was obtained with the Control group. For the Depressive group the initial increase in speed was greater, and was followed in every case by a falling off in efficiency in Session IV (Fig. 2). The difference between the mean scores of the two groups was significant in Sessions I and IV (Fig. 4). Similar curves for accuracy on the Track Tracer test were less distinctive, but in the main the Control group became less accurate over the sessions and the Depressive group more so. It might seem, therefore, that the loss in speed in the case of the Depressive group in Session IV was due to their greater accuracy. This does not seem, however, to be the case, since in this group the correlation between speed and accuracy over the four Sessions was only −0·155, which is not significant. The correlation in the case of the Control group was only −0·393, which is only just significantly different from zero.

In the tests for *Natural Speed of Turning* the Control group produced a steady rate of turning which varied little from Session to Session, although there were comparatively wide individual differences. About the same number of cases increased speed slightly over the Sessions as decreased speed. In the Depressive group, however, every case increased speed between the first and second sessions (Fig. 3). The mean speeds at each session for the two groups were not significantly different. There was, however, a significant increase in the mean speed of the Depressive group between Sessions I and II.

In the test for *Maximum Speed of Turning* there seemed no homogeneity in the scores of either group, although their means were significantly different in Sessions I and III. The technique of giving this test must be improved.

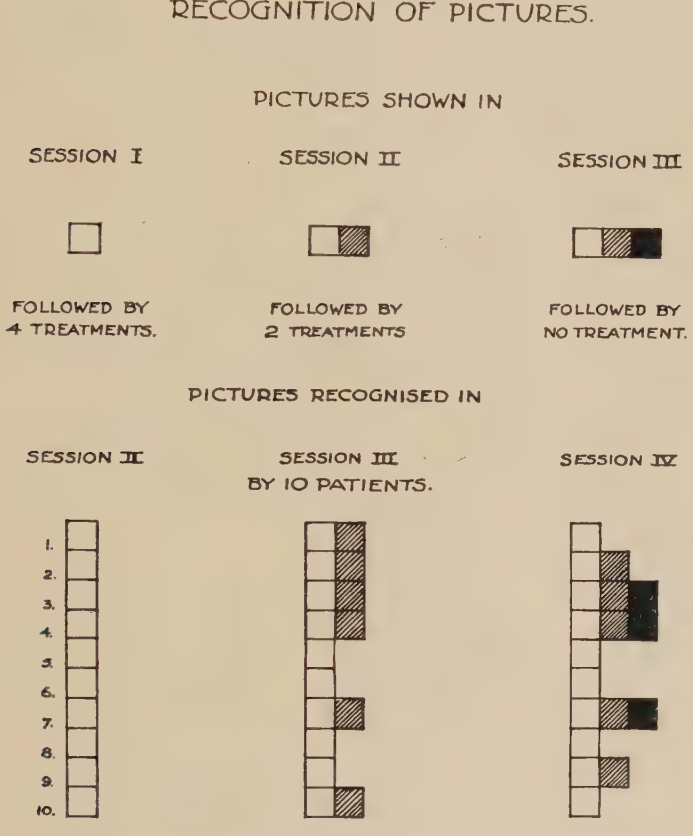


FIG. 5.

*Tests of Retentivity.*

As already stated, these tests were divided into those assessing *Immediate Recognition and Recall*; and those assessing recognition and recall of material assimilated immediately before or during the course of treatment, and recalled or recognized about a week later. These latter tests have been named tests of *Recent Recognition and Recall.*

*The Digit Span Test for Immediate Recall* produced no significant difference between the two groups nor between the four sessions. This was almost certainly due to the insensitivity of the test. For more accurate assessment this test will have to have many more items and a much wider range of scores.

*The Names Test for Immediate Recognition* produced a fall in score in 9 out of 10

cases in the Depressive group in the second Session. A similar fall in every case was noted in the *Picture Test for Immediate Recall and Recognition* of non-verbal material. In neither of these tests did the Control group show any significant variation of mean score over the sessions, and in each case it was statistically differentiated from the Depressive group in Session II.

In the *Story Test for Recent Recall* there was a dramatic, though expected, fall in score in 9 out of the 10 cases in the Depressive group after the beginning of treatment, while the Control group produced the expected learning curve. The mean scores of the Depressive and Control groups were significantly different at every Session. In the test for *Recent Recognition of tests* done in previous Sessions the loss in mean score in the case of the Depressive group was less severe and more quickly made up than in the test for recent recall.

The test for *Recognition of Pictures*, although not psychometrically rigorous, produced some interesting qualitative results, which indicated that the treatment seemed to produce an amnesic effect for some days after its completion (Fig. 5). Pictures which were seen *after* the completion of treatment were forgotten, while the one picture seen *before* treatment was started, was always retained. It seems that, as a result of poor attention, it is the process of assimilation rather than retention as such which is impaired.

## Comments.

The finding of Sherman, Mergener and Levitin (1941) that E.C.T. has no significant effect on memory has not been supported by this investigation, which indicates that treatment seems to have a definite and demonstrable effect on the recognition and recall of material assimilated immediately beforehand. The findings of Zubin and Barrera (1941) that E.C.T. impairs both the recognition and recall, after treatment, of material assimilated beforehand is, however, well supported; and so is their finding, confirmed by Mayer-Gross (1943), that recall of material is affected more than its recognition. This, however, may only be another way of expressing the well-known fact that recognition is an easier process than recall.

The tests used in the present investigation appear to differentiate between tasks involving intellectual activity, such as accurate mental work (i.e., addition) and retention (i.e., names, picture, story) on the one hand, and those involving motor response, such as muscular work (i.e., turning) and hand-eye co-ordination (i.e., track tracer) on the other. The former seem to be temporarily impaired during treatment and the latter to be improved (Fig. 4).

Since there is evidence that it is the process of assimilation rather than retention as such which is affected by treatment, remembering as well as rate of mental work may suffer from the lack of concentration and increased distractibility so characteristic of the patient during treatment. On the other hand, the increase of speed of muscular work which takes place during treatment argues the removal of retardation, which again is a characteristic effect of E.C.T. This would also explain the improvement in hand-eye co-ordination where relatively little intellectual activity is required.

Three lines of inquiry seem to be suggested by these results. The first is to discover more precisely the nature of the temporary impairment manifested during treatment in the tests for intellectual efficiency and retentivity. The second is to ascertain the effects of the removal of retardation on various types of performance. The third is to confirm by more rigorous tests the suggestion that E.C.T. temporarily impairs the process of assimilation rather than retention as such, and to find out how long after the end of treatment such impairment lasts. In this last line of inquiry tests of attention should provide valuable information.

## Summary.

The results of a small battery of tests given repeatedly to 10 depressed patients undergoing a course of E.C.T. and 10 controls suggest that the treatment produces two effects working in opposite directions, namely, a decrease in rate of accurate mental work and a simultaneous increase in the rate of motor response. Which of these two effects predominates depends upon the type of task involved.

Thanks are due to Dr. P. K. McCowan for permission to test the patients, and to Miss M. Houliston for permission to test the control group of nurses. Dr. W.

Mayer-Gross and Mr. J. C. Raven have both contributed invaluable advice on the clinical and psychological aspects of the paper. Thanks are also due to Dr. Hunter Gillies, Dr. W. McAdam and Dr. J. Harper for selecting those of their patients suitable for testing, and to Mrs. E. Beattie for giving the routine tests of intellectual ability.

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# Part II.—Reviews

**Psychotic Art.** By FRANCIS REITMAN. London: Routledge and Kegan Paul, 1950. Price 16*s*.

The artistic products of the mentally ill have been approached from various points of view. As phenomena of expression they have been used as aids to diagnosis and treatment, as a means of investigating activities such as perception, imagination and thinking or even as evidence in attempts to explain certain schools of art. The standpoint of this book is mainly behaviouristic, avoiding by intention the interpretative approaches which are so difficult to verify. The author himself writes: "The aims of this book are to study the special characteristics of psychotic pictorial activity and to investigate its motivation. A psychiatric estimation of art aims to remain a scientific approach and must concern itself with truth only."

The main chapters deal with cognitive disturbances of the personality in relation to artistic expression. Dr. Reitman believes that altered categorical behaviour in psychotics is generally accompanied by disturbance of the body schema and that this is reflected in their artistic products. He marshals clinical, psychometric and experimental evidence which, even if incomplete, give strong support to his views, and he indicates further possibilities of research into various aspects of this interesting subject.

The chapters on the content and nature of psychotic art are followed by illustrative case-histories. In a short final chapter Dr. Reitman examines some cultural factors which influence "modern" artists to paint schizophrenic-like pictures. He points out that cultural influences on schizophrenic paintings are largely unexplored, and that the resemblances between the work of schizophrenic and "modern" artists are more apparent than real.

The bibliographic references and illustrations are well chosen, but it is a pity that it was not possible to reproduce more of the illustrations in colour.

Although the author has deliberately neglected consideration of the affective aspects of personality, the book is an important contribution to our knowledge of symptomatic art and is recommended to all who are interested in that subject.

W. S. MACLAY.

**Schizophrenic Art: Its Meaning in Psychotherapy.** By MARGARET NAUMBURG. London: William Heinemann: Medical Books Ltd.

In recent years there has been an increasing interest in the use of art to help in the understanding and treatment of patients suffering from mental illness. This book shows how valuable it can be in the hands of one who, as Dr. Rennie says in his introduction, has a trained understanding of human motivation and behaviour as well as being an artist. The conception advocated in some quarters of artists being given some kind of uniform training to turn them into "art therapists" seems fundamentally wrong, but if a psychiatrist, an analyst, an occupational therapist or nurse has a knowledge of art it can be usefully employed whatever the particular approach to treatment may be. Miss Naumburg describes the psychotherapy of two schizophrenic patients whose painting and drawing enabled her to achieve a much better understanding of the psychopathology of their illnesses than had been possible with only verbal expression, while through the medium of their painting the patients were helped to resolve their problems. The results appear to have been eminently satisfactory, particularly in the first case.

The importance of art as an aid to verbal expression and as a means of communicating by symbols in a way not possible in rational words is stressed by Miss Naumburg, and discussed in the interesting historical survey of the significance of psychotic and neurotic art which precedes the clinical studies. Examination of the symbolism revealed in the paintings of her two patients and of the use made of them are described and illustrated in the case-reports, which make fascinating reading.

Miss Naumburg contrasts the uniformity of symbols used throughout the ages

with the variety of interpretation given by adherents of differing schools of psychopathology. She thinks that in the proper use of art therapy it is essential to pay more attention to the patients' interpretation of their own symbolic creations rather than to interpret for them.

The book is beautifully produced, with an abundance of illustrations, many of them in colour, to go with the text. It will be of value to those engaged in the field of psychotherapy, and to many others who have an interest in psychopathology and in the nature of creative art. W. S. MACLAY.

**Wisdom, Madness and Folly. The Philosophy of a Lunatic.** By JOHN CUSTANCE. London: Gollancz, 1951. Pp. 254. Price 16*s*.

Mr. Custance, who is now in his early fifties, had had half-a-score sharp attacks of simple mania and acute melancholia since his thirties. He is a man of education, who has read widely in the fields of psychology and philosophy, and who has the individualism, humanity and sensitivity that are so often part of the cyclothymic personality. He writes well and he writes clearly, even though much of his book was written when he was emerging from hypomanic phases.

Unlike some sufferers he has not sought to forget his illnesses, nor has he brooded on them as tragic and wasteful interludes. Instead, he has gloried in the opportunity to examine the unconscious content of his mind, and the relationship of his psychotic phenomena to real events. He has formulated a philosophical "Theory of Actuality," which emphasizes the "reality" of hallucinations and delusions, and leads him to state that the inner experiences of psychotics are different from those of mystics, leaders and prophets only because the latter have the spiritual and intellectual capacities to comprehend and make use of their experiences.

Although the author would certainly assess his theory as the most important part of his book, psychiatrists will value other parts more highly. The clinical descriptions of his manic and depressed states of mind are sensitive and revealing, but even more valuable are his accounts of how and why he reacted emotionally to enforced hospitalization; after reading these there will be few hospital psychiatrists who will not have gained deeper insight into the minds of their patients. Mr. Custance freely admits that when he was manic he must have been a difficult patient; even so he was unlucky in some of the hospitals, doctors and nurses he encountered, and it is sad that he still feels great resentment over the certification procedure he underwent. He makes many practical suggestions for the better organization of mental hospitals, but most of his ideas are already being followed in progressive hospitals. HUNTER GILLIES.

**The Electrical Activity of the Nervous System.** By MARY A. B. BRAZIER. London: Sir Isaac Pitman & Sons, 1951. Pp. 220. Price 25*s*.

The book is intended for students, and covers the field adequately though not exhaustively. It first surveys the electrical changes observed in the axon when an impulse passes, and then proceeds through related topics such as the excitability of nerve, the propagation of the nerve impulse, transmission at synapses, the electrical responses to the stimulation of sense organs, and the cortical responses to peripheral stimulation; finally the author gives a survey of the normal and abnormal electroencephalograms of man.

The descriptions of the various types of electrical activity are well integrated so that the relations can be clearly seen. At all points where further discussion would become too detailed, a well-selected bibliography shows the student where further information is to be found.

No other book presents the same information on this important subject. Dr. Brazier's book can be confidently recommended to those who require an accurate and readable account. W. ROSS ASHBY.

**Principles of General Psychopathology.** By SIEGFRIED FISCHER, M.D. New York: Philosophical Library, 1950. Pp. 327. Price $4.75.

Having devoted nearly two-thirds of his book to describing and classifying isolated concepts of normal psychology and related symptoms of psychopathology, the author says, "This kind of psychology has been called the 'psychology without soul.' It does not satisfy our desire and ambition to understand people, and to gain a close insight into their behaviour."

The rest of the book is not very inspiring either ; which is strange, for the author undoubtedly thinks clearly, has assimilated what he quotes of the work of others, and writes, with a pleasing balance of words, in reasonably short sentences.

This book gives a level-headed introduction to general psychopathology, but is not likely " to stimulate the student to see the problems of this science." The difficulty is that Dr. Fischer has written " An Interpretation of the Theoretical Foundations of Psychopathological Concepts " without the necessary inspiration for such an ambitious work.

C. E. H. TURNER.

**More about Psychiatry.** By CARL BINGER, M.D. London : George Allen and Unwin, Ltd., 1951. Pp. 201. Price 10*s.* 6*d.*

In this book are delightful essays, collected into sections on psychosomatic medicine, psychiatry and the world situation. The essays on psychosomatic medicine are excellent, those on the world situation slightly less so ; but to write sensibly on the world situation is even more difficult than to write sensibly on psychosomatic medicine.

Information, wisdom and humour are in these essays, which are written in good English ; Dr. Binger's book is so rich in content, easily set forth, that one wishes to re-read it.

It is a book for a psychiatrist to give to a medical or lay friend whom he wishes to please and interest in psychiatry. Or, perhaps the psychiatrist would be lucky enough to have a wife who thought to make him a present of this little book.

C. E. H. TURNER.

**Psychosomatics and Suggestion Therapy in Dentistry.** By JACOB STOLZENBERG, D.D.S. New York: Philosophical Library, 1950. Pp. 152. Price $3.75.

This book is not a profound contribution to psychosomatic medicine. The author emphasizes instead, that patients do not look forward with pleasure to being in the dentist's chair. The dentist should therefore make himself presentable and use every possible device of suggestion, including, if need be, hypnosis, to set the patient at ease.

The book is simple, superficial and full of " pep." " It is almost unbelievable how simple it is for the dentist to treat the most neurotic patient if handled properly." The author's writing is sometimes stilted—" In a superficial way, I have touched upon the various segments that make up the whole cycle of integrate phases which will lead to successful practice with resulting contentment."

C. E. H. TURNER.

**New Outlook on Mental Diseases.** By F. A. PICKWORTH. Bristol: John Wright & Sons, 1952. Pp. 296, with 9 plates and 41 illustrations. Price 60*s.*

Dr. Pickworth has long been known as the initiator of a new conception of capillary function in the cerebral cortex, which he has studied for twenty-five years. A clear account of what he has found would therefore be sure of a welcome. His main thesis is that the cerebral capillary is not just a way for metabolites to and from the neuron but is an active agent in the cerebral dynamics, reacting to the patterns of incoming impulses and, by its active changes, affecting the patterns that develop.

The possibility has received little attention from other workers, but it should not be dismissed off-hand. Until recently we have not appreciated in the brain the truly amazing degree it achieves in what the electronic engineer calls " miniaturization." To the anatomist, the fact that the human brain can go into a half-gallon jar is a commonplace—to the designer of calculating machines it is a miracle. The brain works, in fact, on a scale of volume that is about a thousand-millionth part of that of the engineer. This tremendous compression suggests that the brain works with great efficiency, making every possible use of what it already has rather than adding a new part for every new requirement.

Now a fact on which Dr. Pickworth rightly lays emphasis is that while the times taken by the actions of neuron and fibre are measured in milliseconds, the times taken by the subsequent actions of the whole organism are measured in seconds, or even in minutes. To change the time-unit from millisecond to minute there must exist some slowing or delaying mechanism. What could be more suitable than the cortical capillary ? It lies in intimate contact with the neurons, it is sensitive to many influences, it affects, or can be made to affect, the neuron's

activities in many ways, and its natural time-unit is of the right order of size. The thesis, then, is by no means unattractive.

Does Dr. Pickworth establish it ? I have been quite unable to find out ; for the book shows, if it shows nothing else, how necessary it is that an author, before he writes, should make up his mind what he is going to write about, and should then discipline himself ruthlessly to that end. Dr. Pickworth has collected, in his lifetime, a great number of facts, in case they should come in useful sometime, and he has now laid them all before us ; but he has forgotten that myriads of facts, like armies of men, have to be marshalled with great care if they are not to degenerate into chaos. Page after page is filled with snippets, apparently a simple regurgitation *en masse* from the author's note-books and card-indexes. From this undigested material the reader is left to guess as best he can what the author intends to imply. At least one reader gave up the attempt, confessing that he could form no proper judgment whether or not Dr. Pickworth had proved his thesis.

It might seem that so many facts would at least make the book worth while as an encyclopaedia, or as a work of reference ; but testing shows it to be insufficiently accurate. A sentence such as " The wave-length calculates to about five thousand million a second," confusing wave-length and frequency, might be a mere slip ; but unfortunately the book contains innumerable sentences that, though admittedly half true, are also half false, so that any reader who relies on a statement in the book does so at his peril. So much space is wasted on snippets like " Arsenic . . . collects in the hair and skin following medication "—a fact known to every reader of thrillers, and mentioned in the book for no discoverable purpose (even the Index ignores it)—that there is no space for extra facts when they are clearly called for. Of innumerable examples where some qualification should have been added I select one. On page 201 the author quotes H.W. Freeman as authority to show that the schizophrenic's brain is " particularly normal," and he then uses this " fact " without qualification or comment. It seems to me that when a question has been so much disputed an author must, in fairness to his readers, either review it judicially and adequately, or describe it as uncertain, or omit it totally.

My experience in checking references proved most unsatisfactory. One paper is quoted in the book as saying that a reduction of 0·5 in the *p*H increased the threshold by × 20 to × 100, for it supports Dr. Pickworth's thesis. Reference to the original paper showed firstly that this increase occurred in the spinal reflexes only, and secondly that the motor cortex, more relevant to his thesis, showed an increase of only × 2. The author can avoid the charge of deliberate falsification only by pleading guilty to carelessness.

The second reference to be consulted was one quoted by him as evidence for his statement, " Electroconvulsive therapy . . . damages the pancreas . . . " The original paper, it is true, describes three cases with damage to the pancreas after electric shock : a man who was electrocuted accidentally by the mains, and two men who died after being struck by lightning ! It is too late to hope that this review will overtake the book, so I suppose we must now resign ourselves to reading in every text-book of the next decade that E.C.T. sometimes damages the pancreas ; and students, heaven help them, will be failed for not knowing it.

These were the only two references checked, but they were sufficient to show me that I dare not trust any statement the book makes. Then of what use is it to me ? It is not sufficiently complete to be an encyclopaedia, it is not readable enough for a survey, and it is not accurate enough for a work of reference. I cannot avoid the conclusion that the book's value is divorced from its price.

W. Ross Ashby.

# Part III.—Bibliography and Epitome.*

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*Hormone-Treated Cases of Menopausal Psychosis.*

Of 28 cases of psychosis in the menopause which were treated with oestradiol in large doses, 20 became symptom-free, 3 improved substantially and 5 remained unimproved. The improvement began regularly in the second week of treatment. During that week the depression and the anxiety yielded first, later the hypochondria and the psycho-vegetative lability. (Author's abstr.)

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* A number of extracts in this section are reproduced from *Chemical Abstracts*. To the Editors of this Journal we extend our grateful thanks.

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*Emotions and Biochemical Findings in Alcoholism.*

In a combined psychiatric-biochemical study of patients suffering from chronic alcoholism, emotions were determined by one investigator (O. D.) and biochemical studies were carried out simultaneously by the other (M. F. F.). In anxiety the biochemical substance is apparently nor-epinephrine, while in tension cholinergic substances are present. The substance found in the presence of resentment cannot be defined, but it is definitely not acetylcholine. It was found that the alcoholic patients had varying degrees of resentment when an urge to drink was present. Alcohol relieved the resentment and the corresponding substance in the blood disappeared. In a few patients, tension and correlated biochemical substances were also present and were affected by alcohol. Anxiety was somewhat decreased but not completely abolished.

There are no indications that the resentment in alcoholic patients is different from that presented by other subjects. (Authors' abstr.)

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*Inheritance of Manic-Depressive Psychosis.*

1. The diagnosis of manic-depressive psychosis is shown statistically to be less common than formerly, and the definition of the psychosis can be assumed to be less inclusive than before.

2. Figures on discharges and readmissions confirm the cyclical nature of the psychosis.

3. Evidence that women are more severely affected than men is to be found in the earlier age of onset and of first admission and in the greater proportion of affected women.

4. Data on twins show conclusively that heredity is involved in the etiology of the psychosis.

5. The high incidence of the manic-depressive psychosis among the relatives of persons with this psychosis and the difference in frequency of the psychosis in different populations are further evidence for the role of heredity.

6. The frequency of the psychosis is about the same among the parents, sibs, fraternal twins, and children of patients with manic-depressive psychosis. The best genetic explanation for the data is that of a single autosomal dominant gene with incomplete penetrance.

(Author's abstr.)

*The Supplementary Motor Area of the Cerebral Cortex : A Clinical and Experimental Study.*

1. In a relatively small zone of each hemisphere, anterior to the motor area for the lower extremity, there exists an area which yields characteristic responses to stimulation. This area, which we have called the supplementary motor area, is situated almost altogether within the median longitudinal fissure and anterior to the primary motor foot area.

2. The threshold for stimulation of a supplementary motor area in both human subjects and monkeys is a little higher than that for the precentral and post-central regions, and yet the effect is clearly not due to spread of excitation across the cortex to those regions.

3. The results of experimental studies in monkeys are as follows :

(*a*) Stimulation of this region has revealed a motor representation of the contralateral extremities. There is a definite topographic organization which it has not been possible to reproduce in man, perhaps owing to the conditions imposed upon clinical exploration.

(*b*) Inhibition of spontaneous grasping in the opposite hand has been produced by stimulation of the supplementary motor area and removal of the area has resulted in forced (or " reflex ") grasping. Reflex grasping is a specific sign of removal of this particular cortical area in the monkey.

4. In man the results of cortical stimulation are as follows :

(*a*) Vocalization, of a more variable and complex character than that elicited from the lower Rolandic cortex, results from stimulation here.

(*b*) Inhibition of voluntary activity (the test situation was oftenest speech) has been the most frequent effect of stimulation of this area. The patients' descriptions indicate that, although conscious, they were unable to carry out or to continue the prescribed activity.

(*c*) Synergies resulting in the assumption of characteristic postures and in the performance of complex manoeuvres have been produced by stimulation of the supplementary motor area.

(*d*) Pupillary dilation and, less often, cardio-acceleration have been observed. On one occasion arrest of breathing was recorded.

(*e*) A few sensory experiences have been produced, usually a general bodily sensation or one related to viscera.

(*f*) Excision of the supplementary motor area has produced no permanent deficit in maintenance of posture or capacity for movement.

(*g*) Local seizures may be produced by stimulation in this region. These attacks may be considerably more complicated in pattern than simple turning to the opposite side.

(*h*) In general, the supplementary motor area differs from the pre-Rolandic motor area in that stimulation has an effect upon the limbs of the ipsilateral, as well as the contralateral, side of the body.

(*i*) Although each supplementary motor area may exert some motor influence upon all four extremities and the trunk in the maintenance of postures and the carrying out of manoeuvres, the most frequent motor effect of each is to produce contraversion and movement of the contralateral arm. (Authors' abstr.)

*Antidepressive Action of* 5-(1,3-*Dimethylbutyl*)-5-*Ethylbarbituric Acid.*

The problem was to determine whether a barbiturate whose action was primarily that of stimulation of the central nervous system had an antidepressive or a euphorogenic effect in patients with pathologic depression. The stimulating barbiturate chosen for study was the sodium salt of 5-(1,3-dimethylbutyl)-5-ethylbarbituric acid. This drug was given in doses of 50 to 150 mgm. by mouth to 10 patients who were severely depressed.

1. Four of the 10 patients responded with temporary disappearance of the symptoms and signs of depression or became euphoric. Two other patients responded with considerable improvement of their mood. The remaining four patients failed to respond.

2. The antidepressive response to the drug began between one and one and a half hours after its administration. The duration of the response persisted throughout the day and into the evening or the following morning.

3. The drug produced undesirable side actions in six patients. The commonest manifestation was intense itching and flushing of the skin, with considerable perspiration. In addition, there occurred on occasion a fine punctate rash, cyanosis, nausea and vomiting, vertigo and ataxia, tremors and paresthesias, and a probable abortive seizure.

The undesirable side actions preclude the further study of this drug, but its antidepressive and euphorogenic action suggests that other, closely related stimulating barbiturates may be worthy of study. (Author's abstr.)

*Central Nervous Action of Hydantoins, Oxazolidinediones and Thiazolidones.*

1. The 5-alkyl- or aryl- and 5-phenyl-hydantoins are active agents against electroshock convulsions. An additional phenyl or thienyl radical at the 5-position is more effective than a methyl or an ethyl group in enhancing anti-electroshock activity. The introduction of a methyl group at the 3-position results either in no change in anticonvulsant activity with a reduction in hypnotic action or in a decrease of both. The 1-alkyl-5-phenyl compounds are potent hypnotics. A maximal hypnotic and anaesthetic activity is attained with a propyl or an allyl chain at the 1-position.

2. The 2,4-oxazolidinediones are active anti-metrazol$^{R}$, but weak anti-electroshock, agents. In contrast with the hydantoins, the presence of a methyl group at the 3-position increases greatly the anti-metrazol$^{R}$ activity of some of the 5,5-substituted 2,4-oxazolidinediones. In these compounds the phenyl group at the 5-position lends only a slight increase in effectiveness in prevention of electroshock convulsions.

3. The 2-phenyl-3-ethyl-4-thiazolidione and its sulfone are as effective as the active, 2,4-oxazolidinediones against metrazol$^{R}$ and are more effective against electroshock convulsions. (Authors' abstr.)

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*Analysis of Prognostic Factors in Insulin Therapy.*

Seventeen factors are subjected to statistical analysis in an attempt to discover prognostic criteria in insulin therapy.

Thirteen factors, some with certain limits, appear unimportant. These are race, marital status, previous course of electric-shock therapy, religion, number of treatment days, number of coma days, total hours of coma, average daily dose of insulin, highest dose of insulin given, number of insulin convulsions, somatotype, diagnosis, and age of onset of psychosis.

The value of combined therapy could not be determined because of choice exerted in selection of cases.

The response to insulin therapy decreases with age at the time of therapy because of increasing length of the time sick.

Patients who gain over 30 lb. (13·5 kgm.) in weight will do approximately twice as well as those who gain under 30 lb. A hypothesis is advanced to explain this.

Patients sick under one year will do approximately twice as well as those sick over one year. It is suggested that insulin therapy will be given as early as possible in the first year of illness. (Author's abstr.)

*Studies on the Blood-brain Barrier with Radioactive Phosphorus.*

Radioactive phosphorus was given to one group of rabbits intravenously in the amount of 20 $\mu$c. per kilogram of body-weight, and intracisternally to another group in the amount of 1 $\mu$c. per kilogram of body-weight. The animals were killed from 10 minutes to 24 hours after the injections, and the $P^{32}$ content of various parts of the central nervous system was determined.

A maximum concentration of the isotype was reached in the brain 12 to 24 hours after intravenous injection and 30 to 60 minutes after intracisternal administration. After its

injection into the cistern, $P^{32}$ penetrated the cortex and the lining of the ventricles with equal rapidity and accumulated in the brain substance to its entire depth.

The $P^{32}$ deposit in the brain, as compared at the times of maximum concentration, was 20 to 50 times as high after intracisternal as after intravenous administration.

More $P^{32}$ concentrated in the pituitary gland after intravenous than after intracisternal injection.

The role played by the blood-brain and blood cerebrospinal fluid barriers in the distribution of phosphorus is discussed. (Author's abstr.)

*Cytology of Rabbit Neurons After "Malononitrile" Administration.*

Experiments were performed on rabbits to determine the effect of "malononitrile" on nerve cells. Histological comparison of control and experimental animals failed to reveal any changes in Nissl pattern of neurons of the spinal ganglia, spinal cord, and various parts of the brain after administration of "malononitrile" when adequate precaution against post-mortem and fixation artefacts was observed. No change could be detected by ultraviolet photomicrography at a wave length of 2,537 A. (Author's abstr.)

*Unilateral and Bilateral Lobotomy: A Controlled Evaluation.*

In order that the importance of the psychologic influence of operative intervention in the therapeutic efficacy of frontal lobotomy might be evaluated, 33 chronically psychotic patients were studied. These patients received either a unilateral or a bilateral lobotomy by chance selection under conditions in which the extent of the operation was unknown to the personnel responsible for the patients' postoperative care.

Of the 16 patients with bilateral operations, beneficial results were obtained in 11 (68·8 per cent.) six months after operation.

Of the 17 patients with unilateral operations, beneficial results were obtained in only three (17·6 per cent.) six months after operation.

Fourteen of the patients with unilateral operation were subjected to a second-stage contralateral operation. Six months later beneficial results were observed in 11 of them (78·6 per cent.).

It is concluded that (*a*) the psychic trauma of operative intervention is not an important factor in determining the therapeutic benefits derived from a frontal lobotomy, and (*b*) except in rare instances, bilateral operation is necessary for beneficial results in the patient with chronic schizophrenia. (Authors' abstr.)

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*Thalamic Activity in Stupor.*

(1) Thalamic electrograms were recorded in 2 patients who had clinical signs of a mesencephalic lesion. Records were made when they were akinetic, and mute, and on recovery.

(2) Spindles of electrical rhythms were recorded from the postero-lateral region of the thalamus during stupor only.

(3) These episodic discharges, which have not been recorded from the human thalamus in other conditions including coma, were associated with episodic waves in the cerebral cortex.

(4) Spindles were more frequent and their rhythmic character more evident under pentothal anaesthesia, but this abolished the associated cerebral cortical disturbances.

(5) Similar changes have been found by other workers in the thalamus and cortex of cats in which the reticular substance of the mesencephalon has been divided.

(6) The present observations have been related to the results of animal experiment and to the present knowledge of thalamo-cortical mechanisms.

(7) On the basis of this work it is suggested that in akinesis with mutism (stupor), the inactivity results from disturbances in the ascending reticular system, which is concerned in the integration and activation of afferent impulses. (Authors' abstr.)

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*Clinical Trial with Cortisone in the Treatment of Chronic Schizophrenia.*

Six long-term patients with schizophrenic illnesses who had been previously treated with electroshock, insulin and lobotomy manifested improvement and in some cases a complete remission after treatment with cortisone. This study indicates that cortisone and electroshock therapy are synergistic in action, and both result in an adrenal response which seemingly is proportional to the improvement in the patient's mental status. Further basic studies in the relationship between the adrenals and the psychotic illnesses seem warranted as a result of this investigation. (Authors' abstr.)

NOVEMBER.

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*Electrocorticography in Psychomotor Epilepsy.*

1. Current concepts of the origin of psychomotor epilepsy are discussed.

2. Indications and contra-indications for electrocorticography and for surgical intervention in the management of patients with psychomotor seizures are suggested.

3. A simple and efficient method of electrocorticography, which can be used in unscreened operating rooms, is described.

4. Focal spiking from the anterior 4 cm. of the temporal cortex was observed during sleep in 19 of 23 patients. Anterior temporal lobectomy eliminated seizures of psychomotor type in 12 of these cases.

5. The clinical evidence points to a bilateral anterior temporal-subcortical circuit in man, comparable with that already confirmed in lower animals.

6. It is suggested that seizures of psychomotor type may be fired from an area of neuronal injury either within the anterior temporal cortex or within its subcortical connections. In the latter, the contra-indications for anterior temporal lobectomy are illustrated and analyzed in the authors' unsuccessful cases. (Authors' abstr.)

*The Electroencephalogram in ACTH and Cortisone-treated Patients.*

1. In 40 courses of therapy (of 37 patients treated with A.C.T.H. or cortisone) E.E.Gs. were evaluated before and during treatment.

2. The E.E.G. was unchanged in 19 or 47·5 per cent. and showed questionable improvement in 9 or 22·5 per cent. for a total of 70 per cent.

3. The E.E.G. showed marked or definite improvement during treatment in 7 of 12 patients in this series who had abnormal control electroencephalograms. Thus, 32·4 per cent. of the patients had abnormal pre-treatment records and 58·7 per cent. of these showed definite improvement.

4. E.E.G. abnormalities progressed or developed in only four of 37 patients, and in one the abnormal changes were attributed to the progression of the disease process, and not the effect of the hormone.

5. There was no specific E.E.G. correlation with electrolyte changes and mental changes during the treatment.

6. The occurrence of abnormal E.E.Gs. in some patients with rheumatoid arthritis, lupus erythematosus and periarteritis nodosa is noted. (Authors' abstr.)

*The Slow Voltage Variation of Cortical Spreading Depression of Activity.*

The slow voltage variation coincident with the spreading depression of activity, in the rabbit's cerebral cortex, was measured with electrodes inserted into the cortex and the underlying white substance, led against a distant, reference one. The voltage curves obtained were compared with that from an electrode applied to the pial surface, such as has been described previously.

Inside the cortical grey substance a negative elevation was recorded, but, in any given region reached by the response, it appeared later than at the pial surface, and was preceded by an initial positive phase. As at the pial surface, the negative elevation was followed by a final, long-lasting, slowly subsiding positivity. The more deeply the electrode was inserted into the cortex, the later appeared the negative elevation, and also, the lower was its amplitude. Inside the subcortical white substance this negative phase did not occur—the curves presented only the initial and final positive elevations, separated by a recess of the voltage.

The early stages of the voltage variation of spreading depression are remarkably similar to those of the variation induced by prolonged arterial occlusion. It is concluded, therefore, that they are referable to the same events.

It is assumed that the voltages recorded during these early stages may correspond to an electric field of currents established, in the conducting medium, by differences of potential which appear between distinct parts of the surface of neurones. (Author's abstr.)

*On the Conditions for the Recording of Leão's Spreading Depression.*

The following requirements for the optimal recording of Leão's depression were discussed :

(1) The corticogram should be led off bipolarly.

(2) The distance between the members of each electrode pair should be small. For the rabbit 3 to 4 mm. is the maximum distance for recording complete depression.

(3) The leading off conditions should be such that the electrodes pick up only the potentials from their immediate vicinity. When any one of these requirements is not met, the depression may not be seen on the E.E.G. record. It seems possible that in some species the geometry of the cortex and the dimensions of the overlying structures are such that the above conditions cannot be fully met.

Leão's depression is accompanied by a, usually biphasic, slow potential change which precedes the start of the depression by 10 to 40 seconds. When the leading-off conditions are such that the depression cannot be recorded, this slow potential change may indicate the presence of the mechanism underlying the spreading depression.

(Authors' abstr.)

*Electroencephalographic Changes Associated with Experimental Temporary Focal Cerebral Anaemia.*

1. The right middle cerebral artery was occluded in 19 monkeys, in 9 animals permanently and in 10 animals for periods varying from 10 to 50 minutes. During each procedure a continuous cortical electrogram was made, and scalp records were obtained at intervals post-operatively.

2. A decrease in electrical potential occurred within 1 minute following occlusion in all but four animals. This decrease was not proportional to the size of the infarct which subsequently developed.

3. In 9 of the 10 animals with temporary occlusion, some restoration of potential occurred within 30 minutes following the termination of occlusion. In 5 of these the potential returned to the pre-operative level in this period.

4. In about two-thirds of the post-operative scalp records there was a persistent diminution of amplitude over the region of the infarct or over the entire right hemisphere.

5. Slow waves, appearing in only two animals during operation, were consistently present post-operatively in about one-half of the animals.

6. Abnormal rhythmic patterns appeared in two-thirds of the animals, but clinical seizures were observed in only three, whose middle cerebral arteries were occluded for 40 minutes, 40 minutes and 30 minutes respectively. In each instance these seizures involved the contralateral arm and face.

7. Epileptiform activity appeared in the E.E.G. from the contralateral as well as the ipsilateral side in 3 animals. (Authors' abstr.)

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*Children and Radio. A Study of Listeners and Non-listeners to Various Types of Radio Programmes in Terms of Selected Ability, Attitude, and Behaviour Measures.*

1. There is a wide range in the number of children who listen to the various types of radio programmes offered on the air. The number of listeners included in any single programme classification used in the author's study varied from one to 95 per cent.

2. Comedy-variety and crime drama programmes were found to be by far the most popular among boys as well as girls. Over 90 per cent. of the children studied indicated that they listened to comedy-variety and to crime drama programmes.

3. While most children listen to such programmes, the amount of time devoted to them is not always so much as the time spent in listening to other programmes. The availability of programmes is one of the determining factors in the distribution of children's listening time.

4. The relative popularity of programmes among boys in descending order was as follows: Comedy-variety, crime drama, anti-crime, daily adventure, quiz, drama, modern music, sports, news, soap opera, educational, miscellaneous, and classical music.

Programme popularity among girls was as follows: Comedy-variety, crime drama, modern music, drama, anti-crime, quiz, soap opera, daily adventure, news, educational, miscellaneous, sports and classical music.

5. The percentage of listeners included in each classification revealed, in general, more pronounced sex than grade differences. Sex differences were found in all classifications but comedy-variety, crime drama, and news. Substantial grade differences were found in the anti-crime, daily adventure, quiz, drama, modern music, sports, and news classifications.

6. The high percentage of listeners found in the comedy-variety and crime drama

classifications suggests that children as a whole seek and need the tension-releasing experience of radio programmes containing light entertainment and humour, as well as the tension-creating experiences offered by crime drama programmes.

7. Children are less interested in exciting programmes with an openly expressed " crime does not pay " approach than they are in the straight murder-mystery drama. This interest in real mystery programmes on the part of children seems comparable to the great appeal of mystery stories among adults.

8. The high percentage of listeners in the quiz and drama classifications indicates that children do not reject informational and educational matter in programme offerings. When the lack of popularity of educational and news programmes is considered in the light of the popularity of quiz and drama programmes, the conclusion that method of presentation influences popularity seems justifiable. These findings seem to substantiate the conclusion of Katz and Eisenberg that people do not object to educational material if it is presented as entertainment.

9. The very low percentage of listeners found in the classical music classification suggests that pupils in Grades 5–8 inclusive are too immature to have developed an interest in this type of programme. A change in presentation might bring about different results among children.

10. Analysis of the data revealed that in some programme classifications listeners were superior to non-listeners in the observed behaviour and in test performance, while in other classifications they were inclined to be inferior. No differences were revealed in a third group of programme classifications.

11. The most significant and consistent differences between listeners and non-listeners, favouring listeners, were found in the following programme categories : Educational, drama, quiz, comedy-variety, and to a more limited extent, news.

12. Listeners to anti-crime, daily adventure, modern music and soap opera programmes obtained lower scores than non-listeners in several of the areas measured, but the differences between listeners and non-listeners were not as significant as those found in the programme classifications showing desirable relationships. The most that can be said about these programmes is that while they do not seem to contribute anything positive to the listening groups, neither are they harmful to children in general.

13. No differences of any import were found in the sports and crime drama classifications.

14. The test variables revealing the greatest number of reliable differences between listeners and non-listeners were : IQ (as measured by a verbal test), general scholastic achievement, reading, vocabulary, literature, history-civics, science and geography. The number and location of these differences varied with the different programme classifications.

15. Fewer significant differences were found in the following test variables : law attitude, happiness, personal-social adjustment, nervous habits, fears, daydreaming, frustration reactions, and imagination.

16. No important differences between listeners and non-listeners to crime drama, anti-crime and daily adventure programmes were found in measures of nervous habits, fears and daydreaming. This finding suggests that the contention of those who claim that these programmes develop tics, fears and daydreaming in most children who listen to such broadcasts has no basis in fact.

17. The age and sex of the children considered determined to some extent the existence or non-existence of differences in behaviour and test performance between listeners and non-listeners in the specific programme classifications. The implication is that radio programmes have different meanings to children depending upon their age and sex. These findings suggest the need for concentrated studies at specific age levels and for longitudinal studies which might reveal the changing influence and meaning of specific types of radio programmes as children progress through their developmental stages.

18. That differences in behaviour and test performances exist between listeners and non-listeners to specific types of programmes has been established. Analysis of these data, however, revealed that the overlap between listeners and non-listeners was so great that it minimized the practical implications of the results even when statistically significant differences were found.

19. The position taken by the investigator with regard to causation is that habitual radio listening to specific types of programmes is in many instances partly responsible for the differences in behaviour observed, there being an interchange of influence among radio listening, the dimensions of behaviour considered and other possible factors. This position maintains that while age, grade, sex, intelligence, social-emotional adjustment and other factors may account for a child's interest in certain types of radio programmes, the habitual listening to specific types of programmes influences to different degrees, directly or indirectly, the child's behaviour and performance in some areas.

20. The results suggest that if we wish to improve broadcasts, the emphasis should be placed upon making educational, drama, quiz and news programmes more attractive to more children, because here is where the most impressive relationships were found between programme listening and the test variables considered.

21. The principle should be applied that guidance in radio listening is as essential as guidance in any other activity. (Author's abstr.)

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*The Effects of Electroshock Therapy on Mental Functions as Revealed by Psychological Tests.*

A group of 35 hospitalized cases of depression were subjected to an extensive battery of psychological tests both before and after the administration of a series of electroshock treatments. The significant findings may be summarized as follows:

1. Improvement in visual perception, verbal concept formation, and judgment.
2. Improved mental organization, powers of integration, with a diminished preoccupation with details.
3. Improved intellectual control, lessened constriction, and greater efficiency in mental function, i.e., with relation to capacity.
4. Patients seem better able to receive and react to external stimulation, and more likely to be able to handle their external environments with their *intellectual* resources.
5. The treatment effected rather little change in the basic and composite structure of the personality of these patients. The relationship of this finding to the probable incompleteness of the supportive psychotherapy is discussed.
6. The marked body-image disturbances in evidence before shock therapy cleared up as a result of the treatment, with noteworthy recovery of reactivity to heterosexual impulses.
7. Increased strength of grip in both hands.
8. Very little memory impairment noted at all; if anything, many of the patients showed improved memory scores.
9. Vastly improved visuo-motor co-ordination, both under normal conditions as well as under an experimental condition of visuo-motor conflict.
10. Heightened activity of the motor discharge channels, especially by the criterion of speed. Associated with this was the fact that once they got started they found it more difficult to control their motor impulses after shock than they did before shock therapy.
11. Improved capacity to mobilize the emotional resources towards the end of adjustment rather than suffer complete blockage and disorientation under emergency conditions, as was apparent before the therapy.
12. The necessity for adequate follow-up studies, both for clinical and research value, was discussed in the light of the possible effectiveness of the Thematic Apperception Test for prognostic purposes at the conclusion of a course of electroshock treatment.

In conclusion, electroshock therapy, when applied to cases of psychotic depression.

serves to restore intellectual efficiency and orientation as well as render the patient more susceptible to external stimuli, both favourable (therapeutic), and unfavourable (traumatic factors in the home or job situations). This fact, together with their improved sensitivity, affective release and ability to use their emotional energies more adaptively once again, all add up to the clear need for follow-up psychiatric case-work. The Thematic Apperception Test, administered after the patient's recovery from the psychotic episode, lends itself as the most effective psychological device to expose the predominant unconscious conflicts that were probably at work in the pre-psychotic personality. Since the basic personality structure is not materially altered, it is further suggested that the released intellectual and emotional energies must be channelized through satisfying work or avocation and psycho-social adjustment if these individuals are to continue to remain adjustable to the demands of life in the community. (Authors' abstr.)

## J. GENET. PSYCHOL.

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*Adrenergic and Cholinergic Properties of Blood: An Investigation of the Blood of Psychiatric Patients.*

Neither adrenergic nor cholinergic substances are present in the peripheral venous blood of psychiatric patients in sufficient amounts to be demonstrable with an isolated strip of rabbit intestine. This investigation casts doubt on previously published findings that the peripheral venous blood of individuals in certain emotional states contains characteristic and predictable adrenergic and/or cholinergic properties. (Author's abstr.)

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*The Localization of Some Acid Phosphatases in Brain Tissue.*

The histological distribution of acid phosphatase activity has been studied in rapidly frozen and vacuum-dehydrated brain tissue. The main site of enzymatic phosphate liberation from glycerophosphate was in the cytoplasm of neurons. Glial and neuronal nuclei were the main site of adenosine triphosphate cleavage, and adenosine monophosphate was split mainly in nerve fibres. (Authors' abstr.)

*Efferent Connexions of the Human Prefrontal Region, with Reference to Fronto-Hypothalamic Pathways.*

Efferent connexions of the frontal pole have been studied by the Glees silver impregnation method in a case of topectomy of area 10/FE. The findings have been contrasted with a case of rostral leucotomy, aimed at undercutting areas 9/FDm and 10/FE.

Efferent fibre systems arising from the extreme frontal pole are very few. They are confined to a distinct projection upon the dorso-medial thalamic nucleus, some short association fibres to adjacent prefrontal cortex, a few callosal fibres, and a weak contribution to the superior longitudinal fasciculus. There is no connexion with the hypothalamus or any other subcortical centres.

A direct cortico-hypothalamic pathway has been demonstrated originating anterior to the agranular frontal cortex and terminating in the ventro-medial and lateral hypothalamic nuclei. Whether this tract arises from the medial orbital or dorsal frontal cortex cannot be determined from the present material. (Authors' abstr.)

*Cessation of Dreaming After Brain Injury.*

Three cases are briefly reported in which cessation of dreaming was spontaneously described as an after-effect of occipito-parietal brain injury. The locus of the lesion was right-sided in two cases (one of which was a left-handed man) and bilateral, though predominantly left-sided, in one. This loss appeared to be permanent in two cases and temporary in one. Depression of dreaming was associated with impaired visual imagination and memory in the waking state and with residual topographical loss. All three patients were of good pre-traumatic intelligence, and reasonable confidence could be placed in their testimony.

Kindred observations from the literature of visual agnosia are mentioned. It is tentatively suggested that dreaming is likely to be affected only in those agnosic states in which there is appreciable impairment of visual imagery.

Reduction of dreaming as an early sequel of prefrontal leucotomy and the dreamlike states which may be induced in certain cases of epilepsy by temporal lobe stimulation are briefly discussed.

It is tentatively suggested that depression of dreaming and visual imagery in consequence of brain injury may be regarded as a dissolution in some respects analogous to aphasia. (Authors' abstr.)

*An Investigation of the Psychiatric Aspects of Disseminated Sclerosis.*

The findings in a selection of previous reports on various psychiatric aspects of disseminated sclerosis are reviewed. The causes of the discrepancies between these findings are considered.

An investigation was made of 100 patients with disseminated sclerosis and of 100 control patients attending a department for nervous diseases, with regard to premorbid personality, emotional antecedents of the illness, and psychiatric, emotional and intellectual changes following the illness.

No specific premorbid personality type was defined in patients suffering from disseminated sclerosis.

Emotional stress antedating the onset or relapse of disseminated sclerosis was considered to be occasionally of significance.

A significant number of patients with disseminated sclerosis stated that an emotional stress, often of a specific nature, led invariably within the lapse of a minute to an exacerbation of symptoms due to a pre-existing lesion.

Anxiety, hysteria and psychosis were found not to be features of disseminated sclerosis.

Emotional lability and intellectual impairment were found in a significant proportion of patients with disseminated sclerosis, especially in those with marked neurological disability. (Authors' abstr.)

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*Psychological Observations on Psychosurgery Patients.*

Most of the changes which people feared would result if we did surgical operations on the frontal lobes did not happen. Second, the changes which did occur are rather general in nature and may be spoken of as decreases in vigilance, anguish and zeal. Third, we certainly need information as to what happens to these psychosurgery patients during the years after they have been restored to the community. (Author's abstr.)

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## 1. Biochemistry, Physiology, etc.

*Hemicrania. Morris, Gordon.* (*Windsor, Ontario.*) [*Can. Med. Assoc. J.*, **59**, 565–7 (1948).]

A discussion of migraine and of Menière's disease, with reference to the role of histamine and the physiological action of ergotamine tartrate (I), prostigmine, nicotinic acid, and thiamine. Dihydroergotamine is less toxic than (I), and produces less nausea and vomiting.
W. C. Tobie (Chem. Abstr.).

*Effect of Hyperinsulinism on Brain Phospholipide. McGhee, Eva C., Papageorge, Evangeline, Bloom, Walter Lyon, and Lewis, George T.* (*Emory Univ., Ga.*) [*J. Biol. Chem.*, **190**, 127–32 (1951).]

Massive doses of insulin were administered to 24 rabbits; 12 were given no further treatment; 6 were given 0·5 gm. of lecithin 1 hour after the insulin; and 6 were given sufficient glucose to maintain the blood-sugar above a convulsive level in spite of the insulin dosage; 12 untreated rabbits served as controls. Lipide P of the whole blood was not significantly affected by the administration of insulin. Insulin treatments produced a 10 per cent. decrease in the brain lipide P. The decrease was effected in about 6 hours and was not reversed by the administration of lecithin or glucose.
Felix Saunders (Chem. Abstr.).

*Use of Positron-emitting Radioisotopes for the Localization of Brain Tumors. Wrenn, Frank R., Jr., Good, Myron L., and Handler, Philip* (*Duke Univ., Durham, N. Car.*). [*Science*, **113**, 525–7 (1951).]

Administration of the anionic dye tetrasulfonated copper phthalocyanine prepared from metallic $Cu^{64}$ produced focal uptake in the experimentally produced brain injury of mice. Doses up to 100 mgm./kgm. were given to rabbits, mice, guinea-pigs, cats and dogs with apparent impunity. Although the biological half-life exceeds the 12·8 hr. physical half-life of the $Cu^{64}$, after 2 days only 6 per cent. of the injected radio-activity remained to injure tissue. The major route of excretion was via the biliary system. Since the $2\gamma$ quanta resulting from positron annihilation emerge simultaneously and oppositely directed, scintillation counters were designed to operate singly or for coincidence counting of oppositely directed annihilation quanta. A Geiger tube $9\frac{1}{2}$ in. from the radio-activity source with a shield and 6-in. collimator with 1-in. slit gave a relative peak counting rate of 1; coincident scintillation counters with $6\frac{1}{2}$ in. crystalto-crystal distance and no shield gave a relative peak counting rate of 23; and a single directional scintillation counter $9\frac{1}{2}$ in. from the radio-activity source with a 6-in. collimator with a 1-in. slit gave a relative peak counting rate of 47. Complete details of the apparatus and experiments will appear elsewhere.
Wesley H. Hartung (Chem. Abstr.).

*Post-mortem Changes in Acid-soluble Phosphorus Fraction of Central Nervous System. Maleci, A.* (*Univ. Padova, Italy*). [*Arch. fisiol.*, **50**, 18–28 (1950); *cf. Kaplan and Greenberg, C. A.*, **39**, 962.[3]]

The acid-soluble P of rabbit brain was measured immediately upon death and 10 minutes later. There was, respectively, 76·0 ± 1·12 and 76·6 ± 1·56 mgm. per cent. of total acid-soluble P. This was subdivided into *total Ba-pptd. P* of 44·4 ± 0·83 and 44·2 ± 1·14 consisting of inorganic P, 18·0 = 0·76 and 37·5 ± 1·22; the two labile P atoms of adenosine triphosphate (A.T.P.) hydrolyzed off in 10 minutes, 13·8 ± 0·77 and 0·9 ± 0·50; the third P atom of A.T.P. hydrolyzed off in 100 minutes, 1·9 ± 0·12 and 1·7 ± 0·29; residual Ba-precipitated unaccounted for, 5·4 ± 0·80 and 4·1 ± 0·51; total Ba-soluble P of 28·0 ± 0·84 and 29·7 ± 0·96 consisting of phosphocreatine P, 7·5 ± 0·47 and 0 ± 0; Hg-precipitated Ba-soluble P, 5·7 ± 0·81 and 10·5 ± 0·31; and Hg-soluble Ba-soluble P, 15·3 ± 0·66 and 16·4 ± 0·63 mg. per cent. The inorganic P and adenylic P have increased at the expense of the A.T.P. and phosphocreatine P.
H. L. Williams (Chem. Abstr.).

*Penicillin in the Cerebrospinal Fluid. Redfearn, Joseph W. T., Elithorn, Alick, Till, Kenneth, and Ibbott, Fank A.* (*Maudsley Hosp., London*). [*Lancet*, **257**, 652–7 (1949).]

A modification of the capillary-tube serial-dilution method (*cf.* Fleming and Smith, *C. A.*, **43**, 6687*g*) was used to assay 152 samples of cerebrospinal fluid from 111 patients including some with parenchymatous neurosyphilis. A single dose of 0·5 megaunits of penicillin (I) produced a bactericidal-cerebrospinal fluid (I) level in 70 per cent. of the patients. The normal blood-cerebrospinal barrier was permeable to (I). Diseases causing excess protein in the cerebrospinal fluid also caused greater permeability of the blood-cerebrospinal fluid barrier to (I). High concentrations of (I) were found in 3 cerebral gliomatous cysts. Barrier permeability tended to be higher in the aged.
Barbara R. Murray (Chem. Abstr.).

*Changes in the Cerebrospinal Fluid during Pneumo-encephalography. Bickerstaff, Edwin R., (United Birmingham Hospitals, Engl.).* [*Lancet*, **259**, 683–5 (1950).]

The only frequent biochemical change was a decrease in the protein content probably due to dilution of lumbar cerebro-spinal fluid.

BARBARA R. MURRAY (Chem. Abstr.).

*The Presence of Cholinergic and Noncholinergic Neurones in the Central Nervous System. Feldberg, W., Harris, G. W., and Lin, R. C. Y. (Univ. Cambridge, Engl.).* [*J. Physiol. (London)*, **112**, 400–4 (1951).]

Acetone-dried tissue saline extracts were made, incubated and assayed for synthesis of acetylcholine by the method of F. and C. Vogt (*C. A.*, **43**, 747*h*) for a number of tracts and regions of the dog brain and spinal cord, as well as the retina and optic pathway of *Sepia officinalis* (I). Results obtained from the dog brain agreed with the concept that the central nervous system is built up of cholinergic (II) and noncholinergic (III) neurones and that the (II) neurones comprise a considerable portion of the secondary ascending neurones. Results from (I) suggested that in the retina the primary neurones of the cones and rods are (III), and that the choline acetylase of the retina is located in the secondary neurones. The data obtained suggest that (II) and (III) neurones may alternate with each other in some instances. MORRIS ROCKSTEIN (Chem. Abstr.).

*Interaction of Aneurine with Some Drugs on the Neurovegetative System. Dessi, Pietro, and Labo, Guiseppe (Univ. Bologna, Italy).* [*Ricerca sci.*, **20**, 1831–42 (1950).]

Synergism between aneurine (I) and dl-benzedrine (II) 0·08, d-(II) sympatol (III) 0·5, veritol (IV) 0·25, tyramine 0·13, ariline (V) 0·10, aleudrine (VI) 0·10, and mescaline (VII) 0·10, all as gm./kgm. given intraperitoneally (i.p.), was studied in white mice and rats. (II), d-(II), and (V) alone caused intense excitement in a few minutes; the remainder showed no action, and none alone caused death. Combined with (I), all caused death in 15 minutes, (II) and (VI) in 5 minutes. (I) 0·27 with d-adrenaline (VIII) 0·0055, d (II), 0·65, stenamine 0·06, or (VII) 0·042, all as gm./kgm. given subcutaneously, gave no deaths in 60 minutes, but (I) 0·27 subcutaneously with d-(II) 0·066, (III) 0·5, ephedrine 0·11, l–(VIII) 0·003, d–(VIII) 0·0054, (IV) 0·25, or phenethylamine 0·1 given i.p. caused 100 per cent. mortality in 30 minutes. (I) 0·2 gm./kgm. i.p. with tetramethylenediamine 0·88 i.p. caused no fatalities. Cocaine 0·050, yohimbine 0·0166 and ergotamine 0·02 had no effect on the toxicity of (I) and (II). Eserine 0·01 i.p. given 16 minutes before (I) and (II) reduced mortality 52 per cent., but prostigmine 0·00055 had no effect. A sublethal amount of d-tubocurarine 0·00075 with (II) gave 90 per cent. mortality in 10 minutes, and tetramethylammonium formate 0·0178 i.p., nontoxic alone, gave 100 per cent. mortality in 5 minutes with (II) 0·08 i.p., with 0·04 i.p. 70 per cent. mortality. Sparteine methiodide 0·05 likewise gave 90 per cent. mortality in 5 minutes. The use of (I) with quaternary compounds may prove useful in curarization, particularly when eserine is used as an anticurare agent.

WILLIAM F. BRUCE (Chem. Abstr.).

*Relations between Vitamin $B_1$ and Acetylcholine. IV. The Influence of Acetylcholine on the Thiamine Content of the Viscera. Itô, Shinji, and Iwai, Satoko (Nagoya Univ.).* [*Vitamins (Japan)*, **3**, 130–2 (1950); *cf. C. A.*, **45**, 1659*de*.]

When 100$\gamma$ of acetylcholine (I) was administered by hypodermic injection to healthy mice, the thiamine (II) content of the viscera was not changed. When (II) was injected into mice by the same manner the (II) content of the liver was rapidly increased; it was highest after 20 minutes and then gradually decreased. The change of (II) in the brain and in the muscle was less than in the liver, and these increases showed their maximum 30 minutes after the injection and the decreases of (II) in the brain and in the muscle were slower than in the liver. When (I) and (II) were injected simultaneously, the (II) content after 60 minutes was higher than after the injection of (II) alone.

S. KAWAMURA and HIROYASU FUKUBA (Chem. Abstr.).

*Corn Causes Pellagra. Rudolph, W.* [*Med. Monatsschr.*, **2**, 23 (1948); *Chem. Zentr. (Russian Zone Ed.)*, 1948 (**11**) 1317.]

A review of the occurrence of substances in corn (3-acetylpyridine and indolyl-3-acetic acid) which act as antivitamins to nicotinic acid, and the possible role these substances may play in the development of pellagra in persons whose diet consists largely of corn.

M. G. MOORE (Chem. Abstr.).

*Clinical and Experimental Studies of Intracranial Tumors with Fluorescein Dyes with an Additional Note Concerning the possible use of Potassium$^{42}$ and Iodine$^{131}$ Tagged Human Albumin. Moore, G. E., Caudill, C. M., Marvin, J. F., Aust, J. B., Chou, S. N., and Smith, G. A.* [*Am. J. Roentgenol. Radium Therapy*, **66**, 1–8 (1951).]

Na fluorescein has proved to be valuable clinically for the identification of brain-tumor tissue at operation. In experimental animals fluorescein has been used in studies of

disruption of the blood-brain barrier. Radio-active diiodofluorescein can be used to localize brain tumors pre-operatively. Radioactive iodinated albumin and $K^{42}$ have been used as tracer agents; their merits and disadvantages are briefly discussed. Improved instrumentation such as the adaptation of scintillation counters to clinical use should increase the validity of the radio-active dye test. Use of radio-active diiodofluorescein in experiments concerned with disruption of the blood-brain barrier is suggested.

G. L. Clark (Chem. Abstr.).

*The Glucides of Nervous Centers. Baudouin, A. (Univ. Paris).* [*Exposés annuels biochem. méd.*, **2**, 46–62 (1939); *cf. C. A.*, **34**, 1697[5].)

Chemical composition and metabolism are discussed.

W. C. Tobie (Chem. Abstr.).

*The Relationship of the Autonomous Nervous System and Lipide Metabolism. Action of Dibenamine and Atropine upon Fat Deposits in the Liver in Partial Hypophysectomy. Ardy, Cesare, and Montini, Tullio.* [*Atti accad. nazl. Lincei, Rend. Classe sci. fis., mat. e nat.*, **10**, 174–8 (1951).]

Adult male rats weighing 180–220 gm. were partially hypophysectomized. Crandall and Drabkin's technique was used (*C. A.*, **41**, 1741*d*). One lot was used as controls; the other received every second day up to the operation 10 mgm. of *dibenamine* per kgm. body-weight; a third lot received daily until the day of operation an injection of 20 mgm./kgm. of atropine sulfate. Five animals of each lot were sacrificed after 2 and 4, 6 and 10 days respectively. The animals receiving *dibenamine* showed an increased respiratory quotient with values of 0·99–1·07 after 2 days. They did not show a greater oxidation of fats than the controls. Effects opposite to *dibenamine* were obtained with atropine. An inhibition of the lipotropic action of choline took place. Similar results were reported by Cedrangalo and Conte Marotta (*Arch. sci. biol. (Italy)*, **22**, 570 (1936)).

A. H. Koffler (Chem. Abstr.).

*Effect of Potassium and Ammonium Ions upon Glycolysis Catalyzed by an Extract of Rat Brain. Muntz, John A., and Hurwitz, Jerard. (Western Reserve Univ., Cleveland, O.).* [*Arch. Biochem. Biophys.*, **32**, 124–36 (1951); *cf. C. A.*, **42**, 2052*e*).

The stimulatory effect of $NH_4^+$ and $K^+$ upon glycolysis as catalyzed by an extract prepared from a $Me_2CO$ extract of rat brain is most pronounced when small amounts of adenosine triphosphate (A.T.P.) are used, and it becomes progressively less as the A.T.P. concentration is increased. Glycolysis by the extracts is not inhibited by $Na^+$, apparently because of the low apyrase content of the extracts. $NH_4^+$ and $K^+$ have direct stimulatory effects which are not due to antagonism between $Na^+$ and $NH_4^+$ or $K^+$; the same concentration of $NH_4^+$ is required for stimulation whether or not the concentration of $Na^+$ is reduced by substitution of trihydroxymethylaminomethane buffer for $NaHCO_3$. Apparently $NH_4^+$ and $K^+$ maintain A.T.P. in these systems by initiating or accelerating phosphorylation reactions, and preventing the formation of adenylic acid.

*The Effect of Ammonium Ions upon Isolated Reactions of the Glycolytic Scheme.* [*Ibid.*, 137–49.]

In the glycolytic system derived from rat brain $Me_2CO$ powder, $NH_4^+$ stimulates three different reactions: (*a*) the transphosphorylase reaction from phosphoenolpyruvate, (*b*) the phosphohexokinase reaction, and (*c*) the hexokinase reaction. The transphosphorylases are affected differently, depending upon whether adenosine diphosphate or adenylic acid is the phosphate acceptor; in the case of the latter the dependency is particularly marked. A highly active myokinase is present in these extracts, and its activity influences the transphosphorylase reaction to a considerable extent. The phosphohexokinase reaction is stimulated to a greater extent by $NH_4^+$ than is the hexokinase reaction. Triose phosphate oxidase activity is uninfluenced by the presence of $NH_4^+$.

F. Saunders (Chem. Abstr.).

*Neuromuscular Action of Acetaldehyde. Sánchez, Félix Sanz, and Bertrán, E. Castellá (Vet. Faculty, Univ. Madrid).* [*Anales facultad vet. univ. Madrid y inst. invest. vet.*, **2**, 79–89 (1950).]

AcH intravenously injected (at 0·1 to 0·2 mgm./kgm.) had a marked anti-convulsive effect in dogs against electric stimulation, acetylcholine and strychnine injections. Duration of effect was about 30 minutes. Rabbits were protected against cardiazone convulsions by 0·2 mgm. of acetaldehyde per kgm. of body-weight.

George K. Davis (Chem. Abstr.).

*An Atypical Case of Phenylketonuria. Cowie, Valerie A.* (*Fountain Hosp., Tooting Grove, London*). [*Lancet*, **260**, 272–3 (1951).]

In 553 patients examined phenylketonuria was diagnosed in 15, of whom 14 were idiots or imbeciles. The remaining child was normal neurologically, dark in complexion, and had a relatively high mental level. His average daily output of phenylpyruvic acid was about 500 mgm.—only half that usual in phenylketonurics. B. R. M. (Chem. Abstr.).

*Cerebral Blood Flow and Metabolism in Neurosyphilis. The Effects of Penicillin, Induced Fever, and Other Therapeutic Measures. Heyman, Albert, Patterson, John L., Nichols, Fenwick T., Jr., and Jones, Rudolph W.* (*Grady Memorial Hosp., Atlanta, Ga.*). [*Am. J. Syphilis, Gonorrhea, Venereal Diseases*, **35**, 301–11 (1951).]

The $N_2O$ method of Kety and Schmidt (*J. Clin. Invest.*, **27**, 476 (1948)) was used to study cerebral blood-flow (I) and metabolism. The mean (I) and cerebral O consumption (II) were decreased from a normal of 58 and 3·1 c.c./100 gm./min. respectively to 40 and 2·4 in untreated dementia paralytica (III), and to 42 and 2·3 in untreated meningovascular syphilis (IV). The values were within normal range in asymptomatic neurosyphilis (V). There appeared to be a definite correlation between the degree of mental deterioration and the reduction of (II) in patients with (III). (II) increased in (III) following penicillin and fever therapy which was associated with an improved mental state. There was little change in (I) and (II) in patients with (V) during fever induced with typhoid bacterial pyrogen, but patients with (III) showed a mean increase in both. There was little or no change in (I) and (II) during the Jarisch-Herxheimer reaction following penicillin therapy. Nicotinic acid and cytochrome c produced no alteration in (I) and (II) in patients with (III) or (IV). A. Dietz (Chem. Abstr.).

*The Oxygen Supply of the Brain and the Mechanism of Deficiency Effects. Optiz, Erich, and Schneider, Max* (*Univ. Kiel, Ger.*). [*Ergeb. Physiol., biol. Chem. exptl. Pharmakol.* **46**, 126–260 (1950); *cf. C. A.*, **44**, 2626*b*.]

A review discussing the O supply of cells, intracellular O pressure, hypoxia, reversible and irreversible effects of O deficiency and their mode of action.

J. H. Weisburger (Chem. Abstr.).

*A Hexokinase Inhibitor in Nerve. Abood, L. G., and Gerard, R. W.* (*Univ. of Chicago*). [*Proc. Soc. Exptl. Biol. Med.*, **77**, 438–41 (1951).]

Homogenates of nerve, but not of muscle or liver, inhibit brain glycolysis; the inhibition is a linear function of the amount of nerve. Two-thirds of the inhibitor activity of rat leg nerve is in a protein and lipide fraction precipitated at pH 5·3–5·5. From 200 mgm. of fresh nerve, 3 mgm. of the protein and 3 mgm. of the lipide are obtained. This semi-purified fraction loses activity slowly in the cold and almost at once upon heating. The inhibition is specific for brain hexokinase. The enzyme from yeast or liver is not inhibited, and glycolysis of hexose phosphates by brain is not inhibited. Fructose utilization is inhibited half as strongly as that of glucose. Crystallized insulin counteracts the nerve inhibitor. This and its other properties are similar to those of the inhibitor from the anterior pituitary. L. E. Gilson (Chem. Abstr.).

*The Physical Chemical Basis for the Action of Calcium during Nervous Activity. Monnier, A. M.* (*Sorbonne, France*). [*Arch. sci. physiol.*, **3**, 177–87, discussion, 187–91 (1949); *cf. C. A.*, **43**, 1475*b*.]

The inhibitory action of Ca++ towards nerve action is discussed in terms of Ca++ fixation through complex formation by proteins and lipides, and the effect of such fixation on cell permeability and in arresting enzyme carboxylase activity. The reactions are reversible and in constant equilibrium. Removal of Ca is through formation of compounds such as the phosphates. George K. Davis (Chem. Abstr.).

*Glycolysis in the Brain. Lenti, C., and Cafiero, M.* [*Boll. soc. ital. biol. sper.*, **26**, 157–8 (1950).]

Anaerobic glycolysis in nervous tissue extracts is affected by the presence of cozymase and by adenosine triphosphate, but is almost completely inhibited by toluene, whether or not these two activating agents are present. B. A. (Chem. Abstr.).

## 2. Pharmacology and Treatment.

*Treatment of Adults for Epilepsy. (I) Toxic Effect of 5-Ethyl-3-methyl-5-phenylhydantoin. Bailey, Allan A., and Worden, Ralph E.* (*Mayo Foundation, Rochester, Minn.*). [*Proc. Staff Meetings Mayo Clinic*, **24**, 483–6 (1949).]

The pharmacological and therapeutic properties of various drugs, especially mesantoin (5-ethyl-3-methyl-5-phenylhydantoin) (I) are discussed. Although (I) is useful in epilepsy,

it must be used with such precautions as blood-counts and differential counts. Serious toxic reactions may occur months after epileptic subjects have apparently adjusted satisfactorily to (I).

(*II*) *General Principles. Bailey, Allan A.* [*Ibid.*, 486–9.]

The adjustment of the use of anticonvulsive drugs to the pattern of seizures of the individual epileptic is discussed. W. C. Tobie (Chem. Abstr.).

*Excretion of the Methonium Compounds. Milne, G. E., and Oleesky, Samuel* (*Univ. Manchester, Engl.*). [*Lancet*, **260**, 889 (1951) ; *cf. Zaimis, C. A.*, **45**, 2863*g*.]

In persons with normal renal function, most of a 95-mgm. intramuscular dose of hexamethonium compounds was excreted in the urine. After an oral dose of hexamethonium bromide, urinary excretion was only 2·3 per cent. Much of the dose was not absorbed, and some could be recovered from the faeces. Absorption from the alimentary tract varied widely in the same person. In renal failure the drug sometimes accumulates in the blood, and should not be administered to persons with poor renal function. There appear to be no important destructive agents in the body. Destruction in the bowel may occur, but gastric juice and trypsin do not affect the compounds.

Barbara R. Murray (Chem. Abstr.).

*Relationship of Calcium and Magnesium to Effects of Phenobarbital on Oxygen Consumption of Brain Slices. Westfall, B. A.* (*Univ. of Missouri, Columbia*). [*Am. J. Physiol.*, **166**, 219–22 (1951).]

A low concentration of phenobarbital (0·3 mgm. per cent.) in Krebs-Ringer-phosphate medium without Ca decreased the rate of O consumption, while the same concentration of phenobarbital in media containing Ca and Mg caused an increase in the O consumption. Omitting Mg from the medium prevented this increase. A greater concentration of phenobarbital (20 mgm. per cent.) decreased the rate of O consumption of the brain slices. This was unrelated to the presence or absence of Ca or Mg.

E. D. Walter (Chem. Abstr.).

*Further Studies of the Cerebral Chemoreceptor Buffers as Influenced by Vasoconstrictor and Vasodilator Drugs and Veratrum Viride. Taylor, Robert D., and Page, Irvine H.* (*Cleveland Clin. Foundation, Cleveland, O.*). [*Circulation*, **4**, 184–9 (1951).]

Tests were made of the effects of pressor and depressor substances upon the peripheral blood-pressure when the substances were acting upon cerebral chemoreceptors of dogs. The drugs were perfused through the isolated brain when the carotid sinus was inactivated and the vagus nerves sectioned. 9·0 mgm. $BaCl_2$ and 0·15 mgm. nicotine caused hypotension and respiratory stimulation. 0·1 mgm. histamine phosphate caused a pressor reaction in more than three-quarters of the experiments, the rise often being preceded by a slight fall. In the remaining experiments the response was depressor. In some experiments histamine ceased, causing a pressor reaction owing to exhaustion of the chemoreceptor mechanism or to tachyphylaxis ; however, ischemia caused a sharp rise in blood-pressure. 0·25 mgm. mecholyl (acetyl-β-methylcholine) produced a rise in blood-pressure. 3·0 mgm. Veratrum viride (Veriloid) reduced blood-pressure when injected into the isolated circulation if the vagi were intact ; there was no effect if they were sectioned. Veratrum injected into the brain circulation caused a marked fall of peripheral blood-pressure that lasted 2 to 4 hours and blocked the chemoreceptors, so no other drugs injected into the brain circulation influenced peripheral blood pressure, although cerebral ischemia still caused it to rise. Theresa McKee (Chem. Abstr.).

*Action of Adrenaline and Hydergin on Cerebral Circulation. Rothlin, E., and Taeschler, M.* (*Sandoz A.-G., Basel, Switz.*). [*Helv. Physiol. et Pharmacol. Acta*, **9**, C37–9 (1951) (*in German*).]

In narcotized cats and dogs, adrenaline (5–20γ/kgm.) increased the blood-flow through the artery supplying the brain. Hydergin (7–30γ/kgm.) decreased peripheral blood-flow, but did not affect or only slightly decreased cerebral blood-flow. It weakened the effect of adrenaline injected immediately afterwards. L. E. Gilson (Chem. Abstr.).

*The Symptomatic Treatment of Paralysis Agitans with Benadryl. Owyang, Edwin.* [Calif. *Med.*, **72**, 57–8 (1950).]

There is no specific cure for paralysis agitans or Parkinson's disease, but benadryl is beneficial *per se* (probably because of an atropine-like effect), and acts synergistically with parasympathetic-inhibitory drugs. J. Dufrenoy (Chem. Abstr.).

*Treatment of Migraine. Results with Dihydroergocornine Methanesulfonate (DHO–180) and Other Ergot Derivatives. Bercel, Nicholas A. (Cedars of Lebanon Hosp., Los Angeles, Calif.).* [*Calif. Med.*, **72**, 234–8 (1950).]

Relief of migraine obtained with parenteral injections of dihydroergotamine (DHE–45) is as effective as that obtained with the much more toxic ergotamine tartrate. Toxicity of the latter is lessened by the presence of caffeine (as in EC–110). Migraine headaches can be prevented by daily ingestion of 10–15 drops of a preparation containing 1 mgm. dihydroergocornine methanesulfonate per ml. J. Dufrenoy (Chem. Abstr.).

*The Effect of Hexamethonium (C6) as Compared to Procaine or Metycaine Lumbar Block on the Blood-flow to the Foot of Normal Subjects. Schnaper, Harold W., Johnson, Robert L., Tuohy, Edward B., and Freis, Edward D. (Georgetown Univ., Washington, D.C.).* [*J. Clin. Invest.*, **30**, 786–91 (1951).]

Ten normal young male subjects in a constant temperature room were subjected on alternate days to 50 or 100 mgm of hexamethonium (C6). Five of the subjects showed a greater increase in foot blood-flow after C6, while 5 others had a greater flow after regional block. These doses of C6 produce a more marked, and in some cases more complete blockade of the sympathetic outflow to the foot. John T. Myers (Chem. Abstr.).

*Molecular Structure and Anticonvulsant Action. Influence of Ring Substitution in Barbituric Acid and Hydantoin. Mercier, Jacques (Univ. Marseille, France).* [*Compt. rend. soc. biol.*, **144**, 1677–81 (1950).]

5, 5–Diphenylhydantoin, 20 mgm./kgm., protected rats against audiogenic seizures, 5, 5-Dipiperidyl- and 5, 5-dianisylhydantoin had no protective action in much larger doses. For effects of substituted barbituric acids see *C. A.*, **45**, 5809*f*.
L. E. Gilson (Chem. Abstr.).

*Production of Cerebral Changes in Insulin Poisoning. Töbel, Friedebert and Maier, H. (Univ.-Klinik, Wurzburg, Ger.).* [*Z. ges. exptl. Med.*, **117**, 319–30 (1951).]

Daily subcutaneous injection of 4–8 units insulin/kgm. body-weight to dogs of 3 to 12 weeks caused increasingly violent epileptic fits, finally killing the animals; in the later stages luminal moderated the seizures. Vitamin B complex or percorten had no effect. At death considerable liver and brain damage was found.
J. H. Weisburger (Chem. Abstr.).

*Acetaldehyde Content of Blood from Etyhl Alcohol Administration, after Treatment with Tetraethylthiuram Disulfide (Antabuse) in Normal Subjects and Alcoholics. Zubiani, A., and Papo, I.* [*Rass. studi psichiat.*, **39**, 526–48 (1950).]

Twenty normal persons (I) and 60 alcoholics (II) were treated by 0·015–0·03 gm. tetraethylthiuram disulfide (antabuse) (T.T.D.) (pharmaceutical preparations) per kgm. body-weight daily and given wine (1 gm. EtOH per kgm. body-weight daily). The AcH content of blood, determined 0·5, 1·2 and 4 hours after the wine administration (by the methods of Massera, Stetz and Steep-Fricke), was 0·15–0·18 mgm. per cent. in (I) (maximum after 0·5 hours), and 1·55–2·60 mgm. per cent. in (II) (maximum after 0·5, 1 and 2 hours respectively in 14, 46 and 38 per cent. of patients). In 51 of (II) the liver-function tests revealed liver affections. In 25 of (II) treated by the Lecoq-Magnoni therapy, the AcH content of blood, after T.T.D. and wine administration, was found to decrease from 0·53–1·85 (before the therapy) to 0·20–0·70 mgm. per cent. C. Scandura (Chem. Abstr.).

*The Role of the Liver in the Detoxification of Tetraethylthiuram Disulfide (Antabuse). Boyd, Eldon M., and Kingswill, Carloine J. (Queen's Univ., Kingston, Ont., Can.).* [*Am. J. Med. Sci.*, **221**, 444–7 (1951).]

Tetraethylthiuram disulfide (I) given by stomach-tube was more toxic to subtotally hepatectomized rats than to laparectomized, but not hepatectomized, controls. It is concluded that the liver plays a role in (I) detoxication.
Marion Horn Peskin (Chem. Abstr.).

*Convulsions in Adult and Young Dogs after Cardiazole Administration. van Bork, J. J., Dalderup, L. M., and Hirschel, M. I. (Univ. Amsterdam).* [*Acta Physiol. et Pharmacol. Neerland.*, **1**, 533–9 (1950) (*in French*).]

The dose of pentamethylenetetrazole required to produce convulsions in dogs and cats a few days after birth (intraperitoneal injection of a 10 per cent. solution) was about 70 mgm./kgm. The threshold dose progressively decreased with increasing age of the animals until a fairly constant level of about 35 mgm./kgm. was reached in the adult. After bilateral removal of the neopallium in the adult dog the threshold dose was doubled.
W. Donald Graham (Chem. Abstr.).

*Changes of the Copper Content of Blood after Electro-shock.* Ferroni, A. (*Univ. Catania, Italy*) *and Indovina, I.* [*Acta neurol.* (*Naples*), **5**, 291–9 (1950).]

The copper content (I) of blood increased from 79–178 to 101–196γ per cent. in 8 and decreased from 70–183 to 26–152γ per cent. in 6 of 15 patients with schizophrenia 5 minutes after the electro-shock treatment, while after 1 hour there was a decrease in 9 cases. No clear relationship between (I) and the hemoglobin or water content of blood or the Takata-Gross reaction could be found (8 cases). C. SCANDURA (Chem. Abstr.).

*Action of Potassium in Insulin Coma and in Electroshock.* Cicardo, V. H., *and Fontana, A. E.* (*Univ. Buenos Aires*). [*Rev. soc. argentina biol.*, **26**, 217–26 (1950); *Compt. rend. soc. biol.*, **145**, 434–6 (1951).]

In dogs in insulin coma the intravenous injection of KCl causes a transient recovery provided that the coma is not of the irreversible type that would not respond to injection of glucose. Electroshock convulsions and hypoglycemic convulsions ameliorate insulin coma and increase the K concentration of the plasma. L. E. GILSON (Chem. Abstr.).

*Distribution of Thiopental in the Central Nervous System.* Hubbard, Theodore F., *and Goldbaum, Leo R.* (*Army Med. Center, Washington, D.C.*). [*J. Lab. Clin. Med.*, **36**, 218–23 (1950).]

In various areas of the brain and spinal cord of dogs with low plasma levels of thiopental (I) there were no significant differences in (I) concentration. As the plasma level of (I) was raised over 17γ/c.c., increasing differences were found. The tissues, in decreasing order of their contents of (I) were: thalamus, cerebral cortex, medulla, cervical cord and lumbar cord. The distribution patterns were directly related to the plasma concentration of the drug, and were dependent on route of administration, dose and time after injection only in so far as these affected the plasma level. The concentration of (I) in the spinal fluid was lower than in the lumbar cord. It rose almost linearly with increasing plasma concentration, and averaged about 10 per cent. of the plasma level.

M. E. DEUTSCH (Chem Abstr.).